"OBSERVATIONS ON THE CIRCULATION IN THE CAROTID ARTERY OF THE DOG."

by

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I N D E X

This thesis is entitled "Observations on the Circulation in the Carotid Artery of the Dog." It deals chiefly with an accurate study of blood velocity changes which occur in the common carotid artery during the cardiac cycle. The work was begun because it was thought that the usual methods of measuring blood flow could be improved. As the work continued it was discovered that the results could be examined from several different viewpoints. Since each of the aspects will be discussed separately, each section will have its own introduction and no general introduction is offered.

PART I

METHODS

ARTERIAL BLOOD FLOW RECORDING.

In recording blood flow, as indeed in making any other measurement, the method used should affect the conditions it is desired to measure as little as possible. Unfortunately many types of flow recorder alter the physiological conditions to such an extent that the flow records have little relationship to the normal. Therefore, before discussing the various types of flow meters it is of value to examine the ways in which a flow meter may affect the blood flow.

The commonest defect of flow meters is that they present a resistance to blood flow. If this is the case, a drop of pressure takes place across the flow meter and since the pressure is lower in the distal part of the artery, not so much blood will flow through the capillary bed as when no flow meter is present. The resistance can take the form of an actual obstruction or it can be long tubes connected to the measuring apparatus. As a fluid traverses a tube, energy is absorbed in overcoming the friction of the wall, hence the longer the tube the greater will be the pressure drop. Whether or not the artery need be cut to insert the flow meter is very important, for the nerve fibres of the autonomic system are distributed to the periphery along the artery walls. Woollard (1926), demonstrated these fibres by staining with methylene blue. Intramural fibres are especially numerous in the case of the carotid artery (Ranson, 1943). Obviously if these

nerves, which play a considerable part in the control of blood flow in the peripheral circulation, are cut, the circulation along an artery will be affected even if only part of the region it supplies derives its autonomic nerve supply from the arterial nerve plexus.

Flow meters can be divided into two main types, those which record only mean flow rates, and those which record the variations in flow during the pulse cycle. It is not intended to discuss mean flow meters in any detail, but as it is necessary to discuss the present results in relation to the results obtained with these meters, a brief description of some types is necessary. The two most important mean flow meters in present day use are the bubble flow meter and the "Rotameter." In the bubble flow meter, blood is led along a glass tube about one meter in length and then back into the artery. The flow rate is measured by timing how long it takes a bubble to traverse a known length of tube. A good description of bubble flow meters is given by Bruner (1948). Stehle (1932) refined the bubble flow meter by placing the tube over the slit of a moving film camera and photographing the movement of the bubble, thus obtaining a record of the instantaneous flow rate. The bubble flow meter suffers the disadvantages that the pressure drop across it is considerable, that the artery has to be cut, and in use even with a heparinised animal, fibrin is deposited on the tube walls

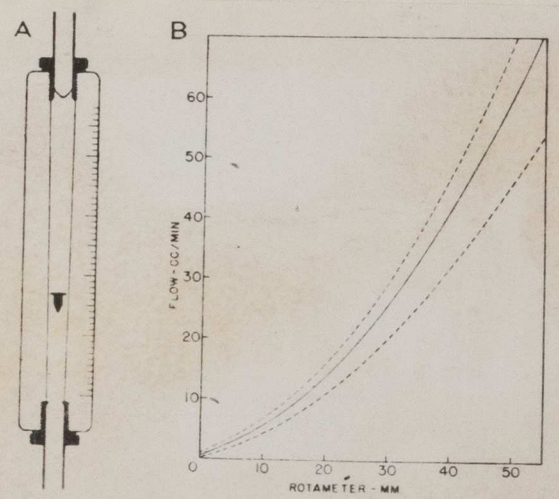


FIG. 1.—*A*, sectional view of rotameter. *B*, sample calibration curves. Solid line curve obtained with blood of average viscosity; broken lines, calibrations with bloods having less and more viscosity than average.

fig 1

which further raises the resistance to flow. The "Rotameter" (Shipley, 1948), consists of a vertical tube slightly conical in bore, inside of which is a light metal or plastic float shaped rather like a top, around the outside of the float is a row of diagonal vanes (Fig.1). The instrument is tied into an artery so that the blood flows into the lower end of the tube and out at the top. As the blood flows through the tube it lifts the float and causes it to spin, the faster the blood flows the higher the float rises. The outside of the tube has graduations calibrated in cc/min. and the flow is read off directly. Further refinements have been made, (Crittenden and Shipley, 1944) in which the height of the float is detected electronically and recorded by mirror galvanometers. This shows fluctuations in flow synchronous with the pulse wave, but the instrument is so heavily damped that they are of little significance. The "Rotameter" suffers from the same disadvantages as to resistance, section of the artery, and fibrin deposition, as does the bubble flow meter. An additional disadvantage is that if backflow takes place the float falls down to zero but cannot measure the amount of backflow.

Many types of flow meter capable of recording variations in flow during the pulse cycle have been devised, but most of them seem to have been put to little use, the most important types of flow meters are the:-

1. Stromborste.
2. Thermostromuhr.
3. Differential pressure flow meters.
4. Electromagnetic flow meter.

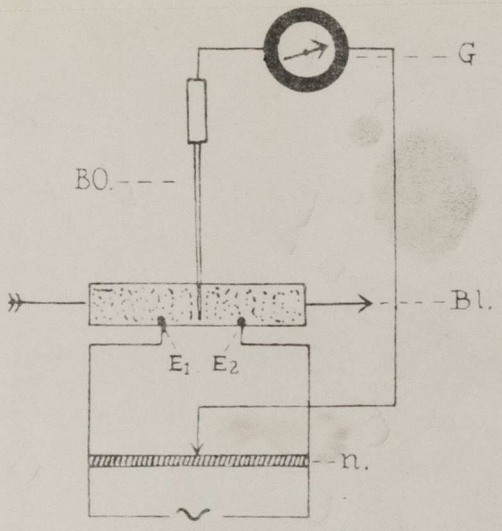


Abb. 1. Schaltungsprinzip der Stromborste. Borste (Bo), Galvanometer (G), Blutstrom (Bl), Elektroden (E1 u. E 2), Brückenpotentiometer (n), Wechselstromquelle (~).

fig 2

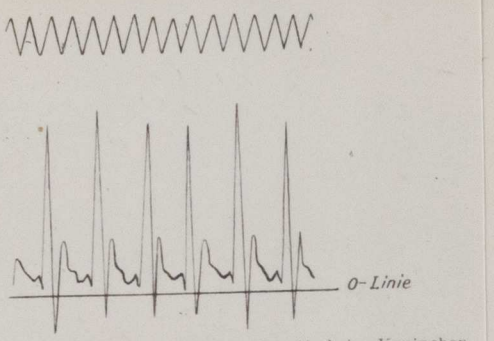


Abb. 7. Geschwindigkeitskurve der Karotis beim Kaninchen.

fig 3.

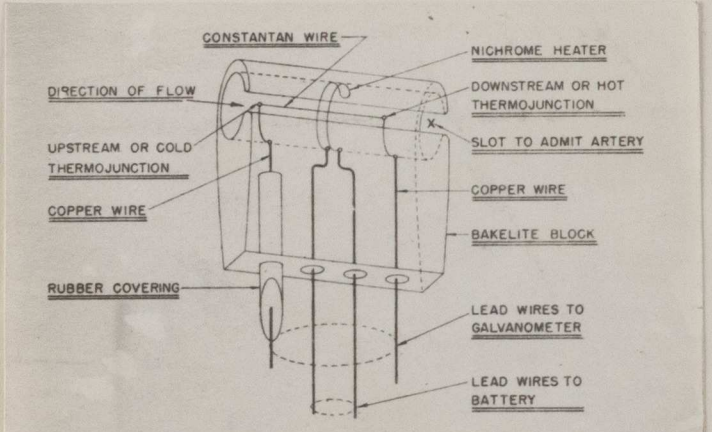


FIG. 1.—Direct current thermostromuhr of Baldes and Herrick.

fig 4

1. The Stromborste or the flow bristle is a modification of the haemodromagraph of Chauveau devised by Holzlohner (1937) and Bergman (1937). The principal of the instrument is that a fine bristle is placed inside the bloodvessel and is deflected by blood flowing past. The deflection is proportional to the flow. In Chauveau's original instrument the deflection of the bristle was measured by connecting it to a tambour, but this led to considerable damping. Holzlohner and Bergman measured the deflection by placing two electrodes one up stream and one downstream of the "bristle", which was a fine wire in a non-conducting tube. (Fig.2). The resistance between the bristle and each of the electrodes acted as two arms of a bridge and the changes in resistance were proportional to the deflection of the bristle. In use the recording head would present little resistance to blood flow, but it would have to be tied into the artery, the difficulty in using the instrument would be that any change in blood resistance would be interpreted as a change in blood flow and further, any fibrin deposited on the electrodes would lead to resistance changes. In designing the instrument great care would have to be taken in choosing the "bristle", for if it was not critically damped it would tend to overshoot or undershoot. In the only figure of arterial blood flow published, the flow in a rabbit's carotid artery (Bergman 1937), the tracing is very spikey (Fig.3) and would lead one to suspect inadequate damping of the bristle. The only other work published using the Stromborste is that of Holzlohner and Schoenerstedt (1940) recording the blood flow

in the jugular vein.

2. The Thermostromuhr was devised by Rein (1928). In the thermostromuhr a small electric heater is placed around the artery and a thermocouple placed above and below the heater. As the blood passes the heater it is slightly heated and this is recorded as a temperature difference between the two thermocouples. It is assumed that the heater gives out a constant amount of heat in unit time and therefore the degree of heating of the blood is proportional to the amount of blood passing the heater, and therefore the temperature difference is proportional to the blood flow, i.e., the greater the difference the slower the rate of flow. In practice the heater which is a small Nichrome coil and the two thermocouples are all mounted in a plastic block which fits about the artery (Fig.4). The great appeal of the thermostromuhr is that it can be placed on a vessel and left in situ and recordings taken from an unanaesthetized animal. In addition the artery does not need to be opened. The thermostromuhr has been used extensively in Germany and the U.S.A. - the American workers have mainly used it as a mean flow meter, but the German school, mainly in Rein's laboratory, have used it as a pulsatile flow meter. In recent years however, the thermostromuhr has become increasingly unpopular as it has been found to be inaccurate. One of the first workers to discard the thermostromuhr was Schmidt (Schmidt & Hendrix, 1938), but the work of Shipley and Gregg (Shipley et al, 1942, Gregg et al, 1942) in attempting to analyse the causes of the inaccuracy in the thermostromuhr has shown that

these are so numerous and variable that it would be impossible to correct for them. They showed that "blood flow values in chronic experiments as read from an in vivo or in vitro calibration, may be highly inaccurate because the relation of the galvanometric deflection to flow will vary with (1) the artery used and its degree of stretch, (2) the position and degree of angulation of the unit with respect to its contained artery, (3) the presence or absence of near zero, zero or back flow in the flow pattern of the metered fluid (5) movements of extra and intravascular fluid in the environment and (6) viscosity of the metered fluid." (Gregg et al, 1942). This formidable list shows that results obtained by using the thermostromuhr must be viewed with considerable caution.

Shipley et al. (1942) conclude that the results obtained from a thermostromuhr are only acceptable when the calibrations have been carried out under conditions identical with those under which the instrument is expected to record; as these are more or less impossible to determine in physiological experiments, the uses of the thermostromuhr are much restricted. In passing, a method somewhat similar to the thermostromuhr might be mentioned; that is the hot wire recorder of Machella (1936). A fine wire of 63 diameter is threaded through the artery and heated by a small electric current; the blood flowing past cools it and changes its resistance, the resistance changes are proportional to the blood flow changes. Calibration is performed with the wire in situ at the end of the experiment. The disadvantages of this method are that it will not record back flow, and if fibrin is deposited on the wire its cooling

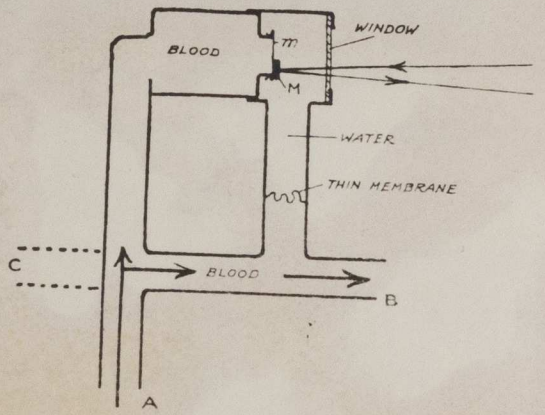


FIG. 432. Principle of the Fleisch Differential Stromuhr. The difference in pressure in the two branches is communicated to the thin membrane manometer, *m*, bearing a mirror M. The outer chamber is filled with water, so that light passing through the window can be reflected from the mirror, and onto a photographic surface, whereby the pressure differences can be graphically recorded. The thin *lax* membrane separates the water from the blood, but does not interfere with the pressure transmission.

fig 5.

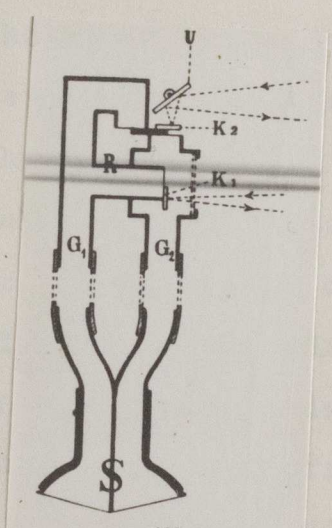


Abb. 5.

fig 6

rate will alter.

3. Differential pressure flow meters. Several different types of differential pressure flow meters have been devised; they all depend on the principle that the pressure drop along a tube of fixed diameter is proportional to the flow rate along the tube. The two types of differential pressure flow meters which are most important are Fleisch's stromuhr (Fleisch, 1920) and the orifice meter. The Fleisch stromuhr is a modification of a much earlier instrument called the Photohaemotachometer (Cybulski, 1890). The form of the instrument is seen in Fig. (5). As the blood flows from A to B a difference in pressure is developed across the membrane m, for in the first branch tube the pressure is due to the momentum plus the blood pressure, whereas in the second branch tube it is due only to the lateral pressure; the pressure difference is proportional to the flow velocity. This instrument can only record undirectional flow; it has several other disadvantages which it shares with the orifice meter. These will be discussed with the orifice meter.

The principle of the orifice meter is that when fluid flows through a constriction in a tube the fluid has to accelerate to pass through the orifice and the accelerated velocity is maintained for some short distance past the orifice. The lateral pressure exerted by the fluid is less below the orifice than above it because of the difference in velocity of the fluid. The pressure difference is porportional to the rate of flow through the orifice. One of the first workers to use the

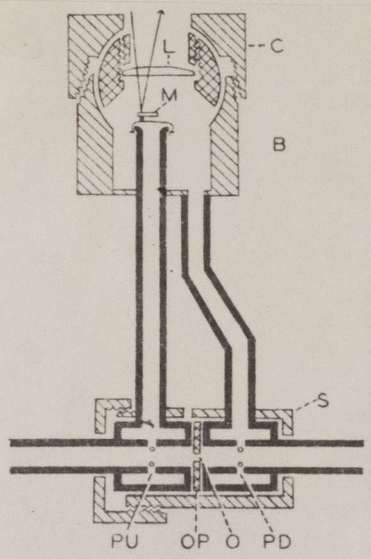


FIG. 2.—Construction details for orifice plate meter and associated differential manometer. *OP*, orifice plate; *O*, orifice; *PU*, upstream, and *PD*, downstream piezometer connections. *S*, shell to hold together component parts of the orifice; slit in shell to left of orifice plate is so constructed that by loosening cap on shell the slit can be slid over orifice plate and plate lifted out without disturbing positions of tubes connected with the piezometer opening. *B*, base of differential manometer; *L*, lens carried in a ball; *C*, cap which holds ball in place. Lens serves as window of manometer. *M*, mirror attached to rubber diaphragm of manometer.

fig 7

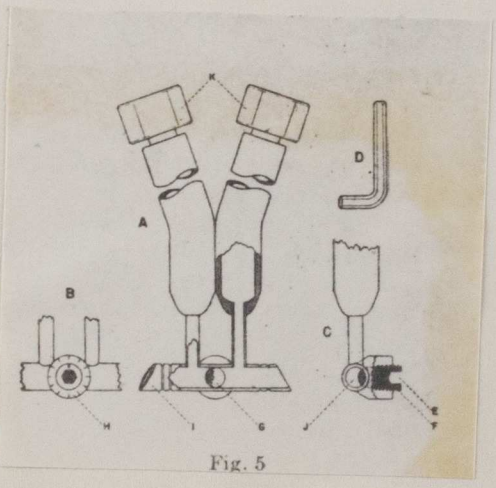


Fig. 5

fig 8

orifice flow meter principle was Broemser (1928). A diagram of the instrument he used is shown in Fig. (6), the orifice was made by indenting the wall of the artery and the lateral pressures recorded through the arterial wall; the instrument had to be calibrated in situ. This must be a difficult instrument to use for slight movements of the vessel would cause artefacts and invalidate any calibration. The orifice meter has been used a great deal by the School of Green in the U.S.A. The form of a typical orifice meter used by Green is shown in Fig. (7). This instrument is tied into the artery and the orifice is a hole in a plate - the plate can be removed for cleaning or for altering the sensitivity of the meter. A simplification of the orifice meter which has been much used was devised by Shipley et al (1943) (Fig. 8); the orifice in this case is made by a screw protruding into the bore of the flow meter tube; the screw is adjusted to obtain the "desired sensitivity."

In their writings, Green and his followers have set the orifice meter up as the standard against which the performance of any other flow meter is measured. This attitude has, it seems, tended to blind them to the imperfections of the orifice meter. In view of this, it is necessary to examine carefully the advantages and disadvantages of the orifice meter. Although the orifice meter is small, though it can be applied to arteries in many different parts of the body with comparative ease, though records are as easy to obtain as with an ordinary membrane manometer and though it will record back

~~flow.~~

flow. The flow meter depends on resistance to flow, its calibration is difficult, its sensitivity is affected by the deposition of fibrin, the recording manometer must be very carefully designed and the bloodvessel wall must be cut in order to insert it.

Sufficient has been already said about the disadvantage of cutting the artery to insert a flow meter. The resistance offered to flow by the orifice meter must be considerable. For instance, Green (1948) recommends that the orifice should be half the diameter of the tube. The pressure drop across a tube of unit length is inversely proportional to the fourth power of the radius of the tube (Poiseuille's Law). From this it will be seen that the mean flow recorded by the orifice meter must be less than that under normal conditions. Calibration of the orifice meter presents several difficulties, the first is that the calibration has to be constantly checked because fibrin is deposited at the point of constriction in the tube. It is difficult to work out a mathematical relationship between flow and the differential pressure developed in an orifice meter. Green (1948) states that the differential pressure (p) is equal to a constant (K_1) times the flow rate(f) plus another constant (K_2 times the flow rate squared (f^2) i.e. $P = K_1 f + K_2 f^2$. The first term is due to friction and is greatly influenced by viscosity and the second is due to velocity and is not influenced by viscosity. From this it is evident that the calibration curve is not linear and its

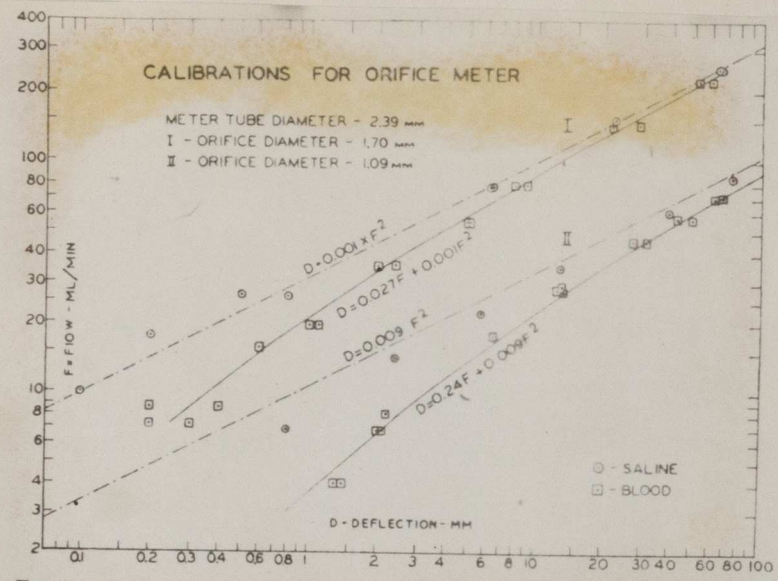


FIG. 3.—Calibrations for an orifice meter, using saline and blood and two different orifices. Dot-dash line, ideal line representing relationship between flow (ordinate scale) and differential pressures, i.e., deflection of recording beam (abscissal scale). Solid line, curve drawn in attempt to match observed points for blood.

fig 9

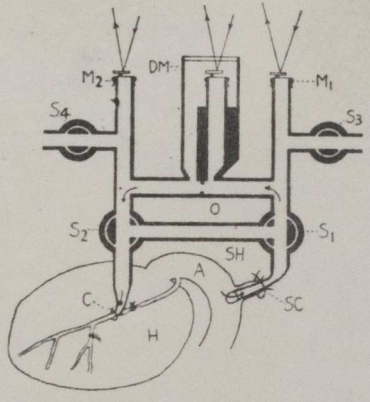


FIG. 4.—Assembly for using the orifice meter for measuring coronary blood flow. *DM*, differential manometer; M_1, and M_2, pressure manometers (M_1 can usually be omitted); S_3, stopcock for admitting blood from a reservoir; S_4, stopcock for allowing blood to flow out with a graduate for calibrating meter; S_1 and S_2, stopcocks for allowing blood circulation to heart through shunt *SH* while calibrating orifice; *SC*, cannula inserted in subclavian artery; *C*, cannula inserted in distal stump of coronary artery. (Reproduced by courtesy of *American Heart Journal*.)

fig 10

and its precise values are difficult to forecast, for the constituents are different for different orifices. Fig.(9) shows a calibration curve from Green (1948). It will be seen that the instrument must be calibrated in vivo and with blood. This need for frequent calibrations in vivo frequently leads to the necessity for a more cumbersome instrument (Fig.10) which overcomes the mechanical simplicity of the original instrument and adds to its resistance to flow. It seems that Shipley et al (1943) do not calibrate their flow meter except at the end of the experiment; this without a doubt leads to inaccuracy in the figures for flow which they quote.

A factor in the orifice flow meter which can lead to grave sources of error in the form of the flow wave recorded is a badly designed manometer. The frequency response must be adequate to follow the rapid changes in velocity during the pulse cycle, and it must be also critically damped. The frequency response of the differential manometers used differs. Green (1948) states that his manometer has a resonant frequency of 25-50 cycles/second. This is a little low. Shipley et al (1943) give a resonant frequency of 90-120 cycles/second. This is adequate. (A fuller discussion of the frequency response of manometers is given in the section on pressure recording p.18)

One final point about the orifice meter; all the workers who use it state that they alter the size of the orifice until the desired sensitivity is achieved. As different sized orifices are likely to alter the form of the velocity pulse

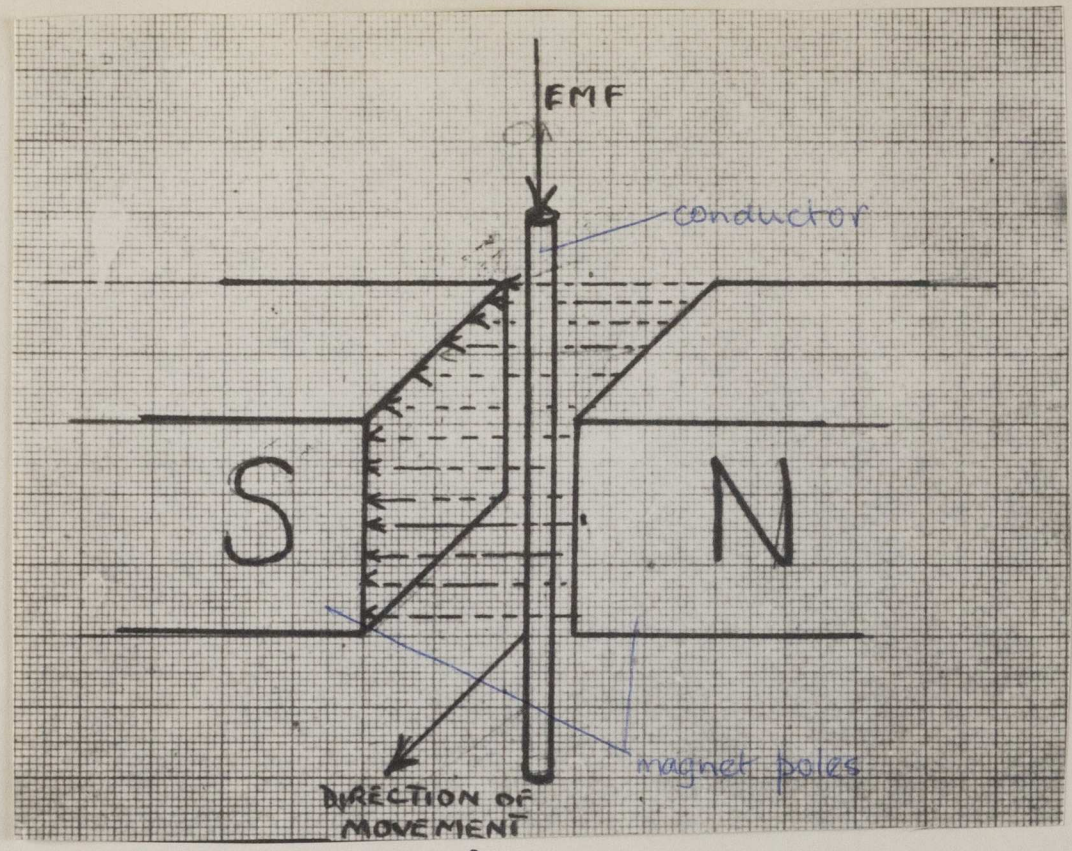


fig 11

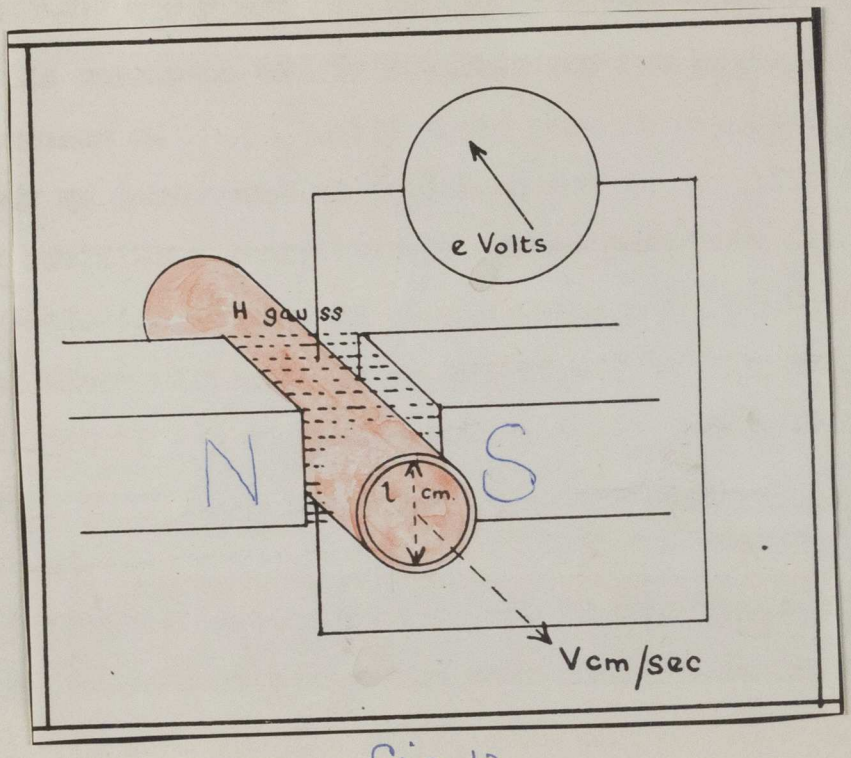


fig 12

wave, a worker is liable to alter the size of orifice until a pulse velocity wave is recorded which has the form that he thinks it should have.

4. Electromagnetic flow meter. The electromagnetic flowmeter was first described by Wetterer (1938) and Kolin & Katz (1938). The flow meter depends on the principle of electromagnetic induction. When a conductor moves through a magnetic field an electromotive force is induced across it. The induced E.M.F. is proportional to the length and velocity of the conductor and the strength of the magnetic field. Blood is a conductor, therefore if it flows through a magnetic field an E.M.F. is induced across the blood. The walls of an artery are conductors, therefore if an artery is placed in a magnetic field and blood flows along it, the induced E.M.F. is conducted to the outside of the artery. From this it can be seen that if only the velocity of blood flow is allowed to vary, the induced E.M.F. is proportional to the velocity of blood flow.(figs.11, 12).

The magnitude of the induced E.M.F. is expressed by the following formula:- $E = H.l.v. 10^{-8}$ where H is the magnetic field strength in gauss, l is the length of the conductor in cms. and v = velocity in cms/sec.; the E.M.F. induced, the magnetic field and the movement of the conductor all must be at right angles to each other (Fig.11, 12). When measuring blood flow the length of the conductor is determined by the arterial diameter, and under normal physiological conditions this changes during the pulse cycle, so that in the electro-

magnetic flow meter, part of the artery in the magnetic field is enclosed in a cuff which maintains the artery at its diastolic diameter. The cuff usually holds the electrodes which pick up the induced E.M.F. and lead it to the measuring instrument.

The advantages of the electromagnetic flow meter are that the artery is not cut, that the calibration curve will be a straight line passing through the origin, that the meter should respond to very rapid changes in velocity, and with a suitably designed electrical recording system it should be inertialess and therefore should not need damping. (In Kolin & Katz instrument the induced E.M.F. modulates a 60 cycle/sec. carrier wave and therefore is limited to a frequency somewhat below 60 cycles/sec.) The factors controlling the induced E.M.F. are known and can easily be controlled. The possible sources of inaccuracy are that the cuff around the artery affects flow - this is the reason that Shipley et al (1943) put forward to explain the difference between the records obtained with the electromagnetic flow meter and those they obtained with the orifice meter. Shipley & Gregg (1944) show that slight constriction of an artery can seriously affect flow through it. It is known that fluids do not flow at a uniform velocity throughout an artery, therefore the E.M.F. detected at the periphery may not reflect the velocity at the centre of the artery and further, this affect may alter at different velocities. Changes in the constitution of the blood and artery wall may affect the E.M.F. induced.

The instrument is calibrated in vivo by perfusing through the artery known volumes of blood or saline and measuring the resultant E.M.F.; the volume flow is proportional to the area enclosed by the velocity curve. This mode of calibration is necessary since the actual internal diameter of the artery is not known and it also allows for any effect the artery wall may have.

It was decided that, the flow meter which seemed most likely to give results which would correspond closest to the physiological conditions existing in arteries was the electromagnetic flow meter. A flow meter was built, the following section details the design of the instrument and the tests carried out upon it.

THE ELECTROMAGNETIC FLOW METER.

Two types of electromagnetic flow meter have been designed:- the A.C. type,(Kolin & Katz, 1938, Kolin, 1945) and the D.C. type (Wetterer, 1938, Jochim, 1948). The A.C. type has an electromagnetic energized from a source of alternating current usually at mains frequency. Therefore the induced E.M.F. takes the form of a mains frequency carrier modulated by velocity variations; this has the advantage that condenser coupled amplifiers can be used and that the electrodes for picking up the E.M.F. need not be nonpolarizable, but a serious disadvantage is that the frequency response is limited by the frequency of the power supply to the magnet. The D.C. type of flow meter has either a permanent magnet or an electromagnet~~io~~ supplied with D.C.; the advantage of this type is that its frequency response is limited to that of the recording

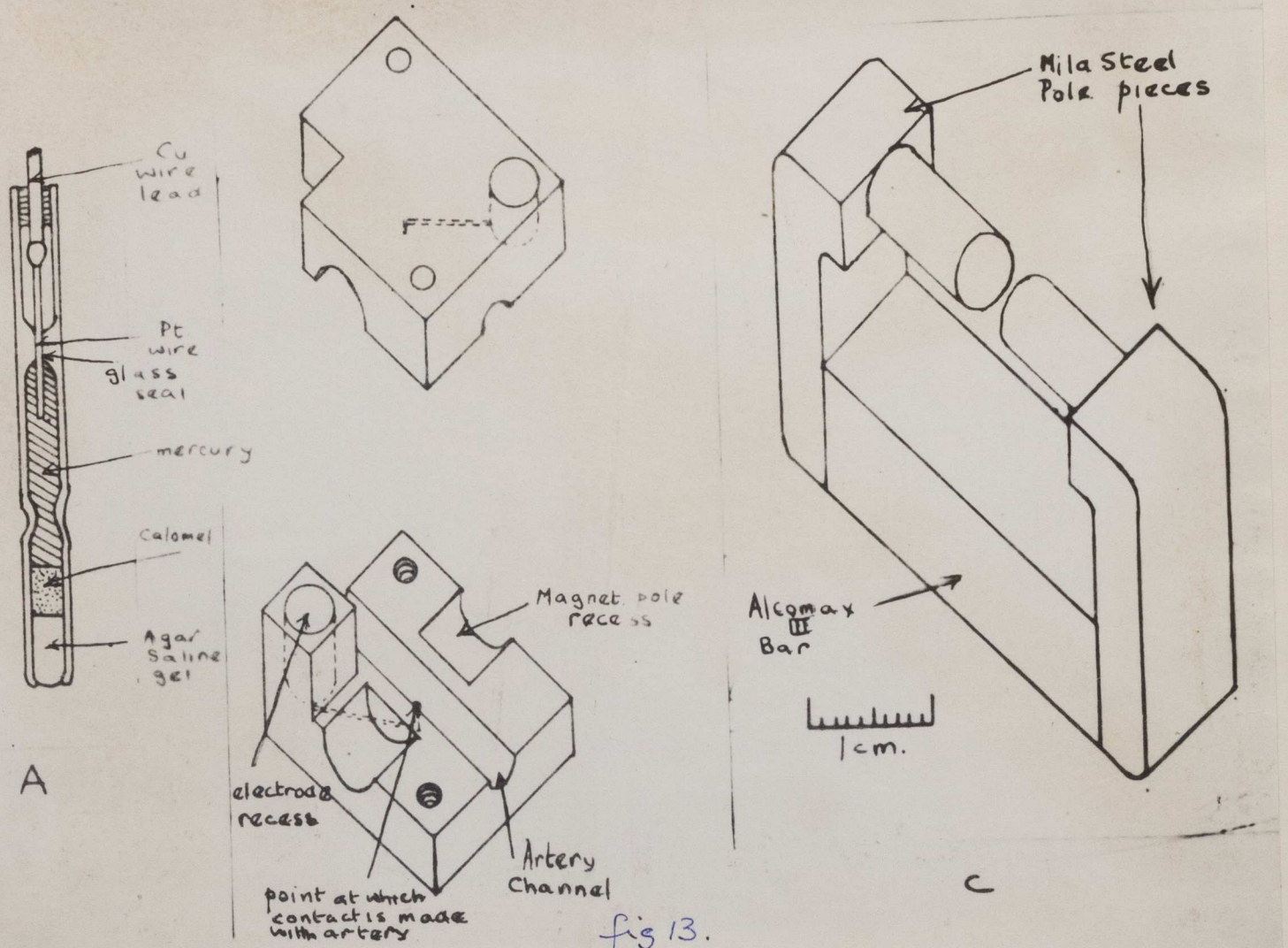


fig 13.

A = Diagram of Electrode B = Diagram of Cuff C = Diagram of Magnet

Cuff + Magnet are drawn on an isometric projection

The same applies to A, B + C.

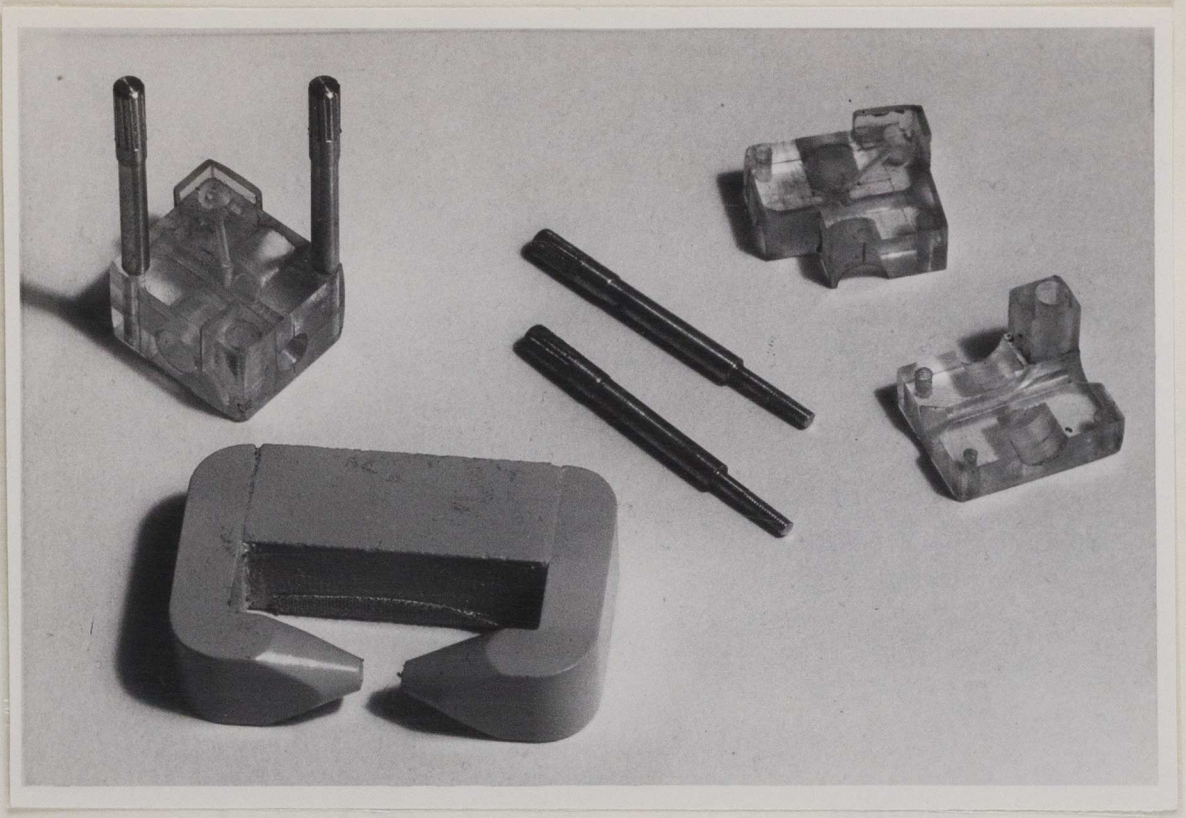


fig 14
for key see fig 13.

apparatus, but the disadvantage is that it requires a stable high gain D.C. amplifier. Shipley et al 1943, have criticized the electromagnetic flow meter on the grounds that its frequency response is inadequate, so that it was decided to build a D.C. type flow meter with a high frequency response.

The essential parts of the D.C. type electromagnetic flow meter are:-

1. An arterial cuff.
2. A magnet.
3. Non-polarizable electrodes.
4. Electrical recording apparatus.

The Magnet.

Previously, electromagnets were used most commonly in electromagnetic flow meters, because the permanent magnets obtainable were not very powerful and were larger. Powerful electromagnets are also rather bulky, and dissipate a certain amount of heat, but even with these disadvantages they were more powerful and reliable than permanent magnets. Recently, with the introduction of new magnetic materials, small, extremely powerful permanent magnets have become available. Two of these alloys are Ticonal, and Alcomax III. The makers of these materials - Messrs. Mullards and Messrs. Jessops respectively - made special magnets for this work. The Alcomax III magnet was slightly smaller and more powerful than the Ticonal magnet, and has been used exclusively in this work. The magnet has the dimensions shown in Fig. (13) and has a field strength of approximately 2,000 gauss. It has been found necessary to cover the magnet with a thin rubber finger stall, for, unless this is done, considerable instability is

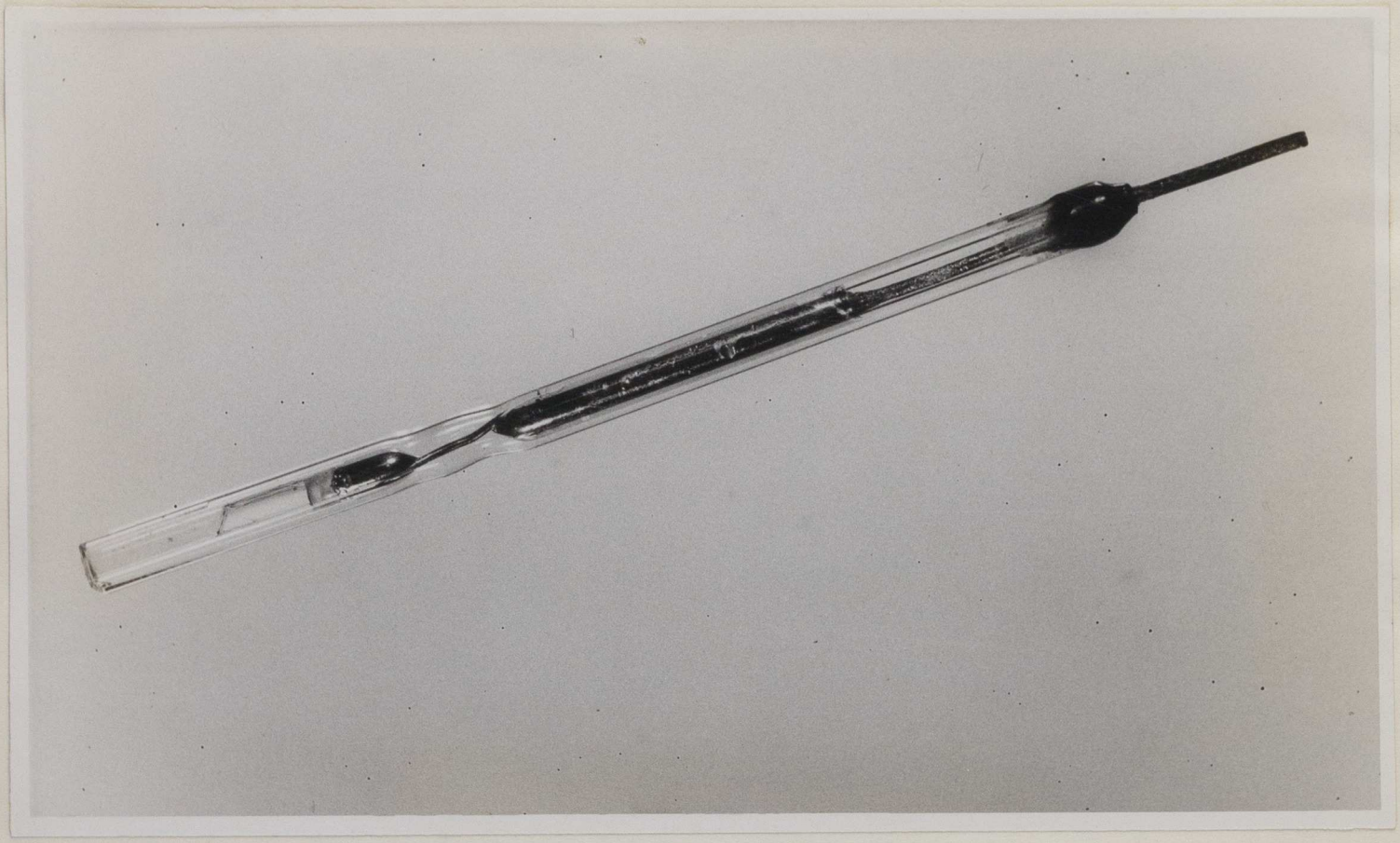


fig 16
for key see fig 13.

experienced with the electrical recording system. Since the cuff clamps tightly about the magnet poles, the cuff and electrode assembly is supported by a brass clamp holding the magnet. It is possible that a clamp made of a ferrous alloy would distort the magnetic field.

The Electrodes.

The electrodes used to pick up the induced potential difference must be non-polarizable. In previous work three types have been used - Calomel half cells, Zinc - Zinc Chloride and Silver - Silver chloride electrodes. The first two types of electrodes are very bulky so it was decided to use silver wire electrolytically coated with silver chloride. However, these electrodes proved very unreliable for it was often found that, although they worked perfectly at the beginning of an experiment, suddenly, for no apparent reason they became polarized and it was found that use of the balance control on the amplifier could not offset the spurious potentials set up by the electrodes. It was then decided that calomel half cells should be tried. The first types tried were the conventional laboratory types, and connection to the cuffs was made through lengths of polythene tubing filled with agar-saline gel. These electrodes proved to be very stable but their large size picked up a proportionately large amount of mains hum which swamped the signal. To overcome the objection to the size of the calomel half cells some miniature cells were devised (Fig.16). These were found to be as stable as the larger cells, and did

not pick up an appreciable quantity of mains hum.

To make the miniature calomel half cells, soda glass tubing of 3mm. external diameter is used for the envelope. A small piece of platinum wire about 1.0cm. long is fused into the bore of the tubing by shrinking the glass on to it,

Both ends of the wire must be free from glass. About 5mm. above the wire a constriction is made in the tube, leaving only a narrow bore about 0.5mm. in diameter; the tube is then cut off about 1.0cm. above the constriction. To fill the electrode, pure mercury (Analar) is first pipetted into the tube above the constriction, and the tube flicked as if it was a clinical thermometer, thus forcing the mercury into contact with the wire and filling the space between the wire and the constriction. No air must remain. Sufficient mercury is put into the tube to come just above the constriction; the purpose of the constriction is to keep the mercury in place. The space above the mercury is now filled with normal saline. A watery paste of pure mercurous chloride is rubbed up with a little mercury. (This is said to make the cells more stable, Clarke, 1928). The paste is transferred with a flattened piece of platinum wire ~~and mixed with normal saline~~ into the saline in the tube. If the electrode is held upright the calomel very quickly settles on to the surface of the mercury. Enough calomel is put into the tube to form a layer about 0.75cm. thick. The calomel is compacted by centrifuging the tubes, to leave a layer of calomel on the mercury, with a layer of saline above. To complete the cells, a 10% solution of Agar Agar in normal saline is prepared and

drawn up into a hypodermic syringe fitted with a fine needle (No.18 or 20). Then, with the tube held vertically, the needle is placed just beneath the surface of the calomel paste and the upper part of the calomel and the saline above it are displaced by jelly. Sufficient jelly is pushed into the electrode to make a clear layer of jelly with no calomel in it above the calomel layer. This manoeuvre is important, for if a layer of saline is left between the jelly and the calomel, on turning the cell downwards the calomel will sink through the saline layer, and leave only saline in contact with the mercury and the cell will be useless. The electrodes are left until the jelly has set and then they were stored with the tips immersed in saline.

In use, contact is made with the platinum by placing a drop of mercury in the upper part of the electrode and dipping into it a piece of copper wire. An alternative is to use Woods metal with the lead soldered into it by melting in boiling water. This, of course, must be done before the electrode is filled; however, these electrodes tend to break owing to the strains set up by the Woods metal.

If the electrodes are used immediately after they are made they will be found to be rather unstable. When they have been left to stand for about ten days they exhibit a high degree of stability, although a few electrodes in any batch are found to be noisy, and must be discarded.

When the stability of the amplifier was being investigated the physical characteristics of the electrodes were also investigated since it was thought that they might be changing

and give rise to instability. Two factors were investigated, the resistance and the potential difference between pairs of electrodes. The resistance of the electrodes *in situ* in assembled cuffs filled entirely with agar saline jelly was measured with a Mullard type resistance bridge and was found to be in the region of 10,000 ohms. with different pairs of electrodes, and it remained constant for each pair of electrodes. The calomel half cells is so called because it exhibits a potential difference against a hydrogen electrode when they are placed in a conducting solution. The potential difference is 0.56 volts (Lehfeldt, 1908), using normal KCl, although in the case of the miniature electrodes used here the P.D. would be different, but it should remain constant. A hydrogen electrode was not readily available as a standard, but as the electrodes were used in pairs the potential existing between pairs and its variations, if any, was of importance. The potential difference existing between pairs of cells was measured with a Cambridge Instrument Company dial potentiometer, and it was found that the potential difference between different pairs varied between 2-14 millivolts. This potential difference remained constant over several hours. The potential difference between the electrodes was not of any importance in this instance, for by using the balance control of the amplifier the potential could easily be offset.

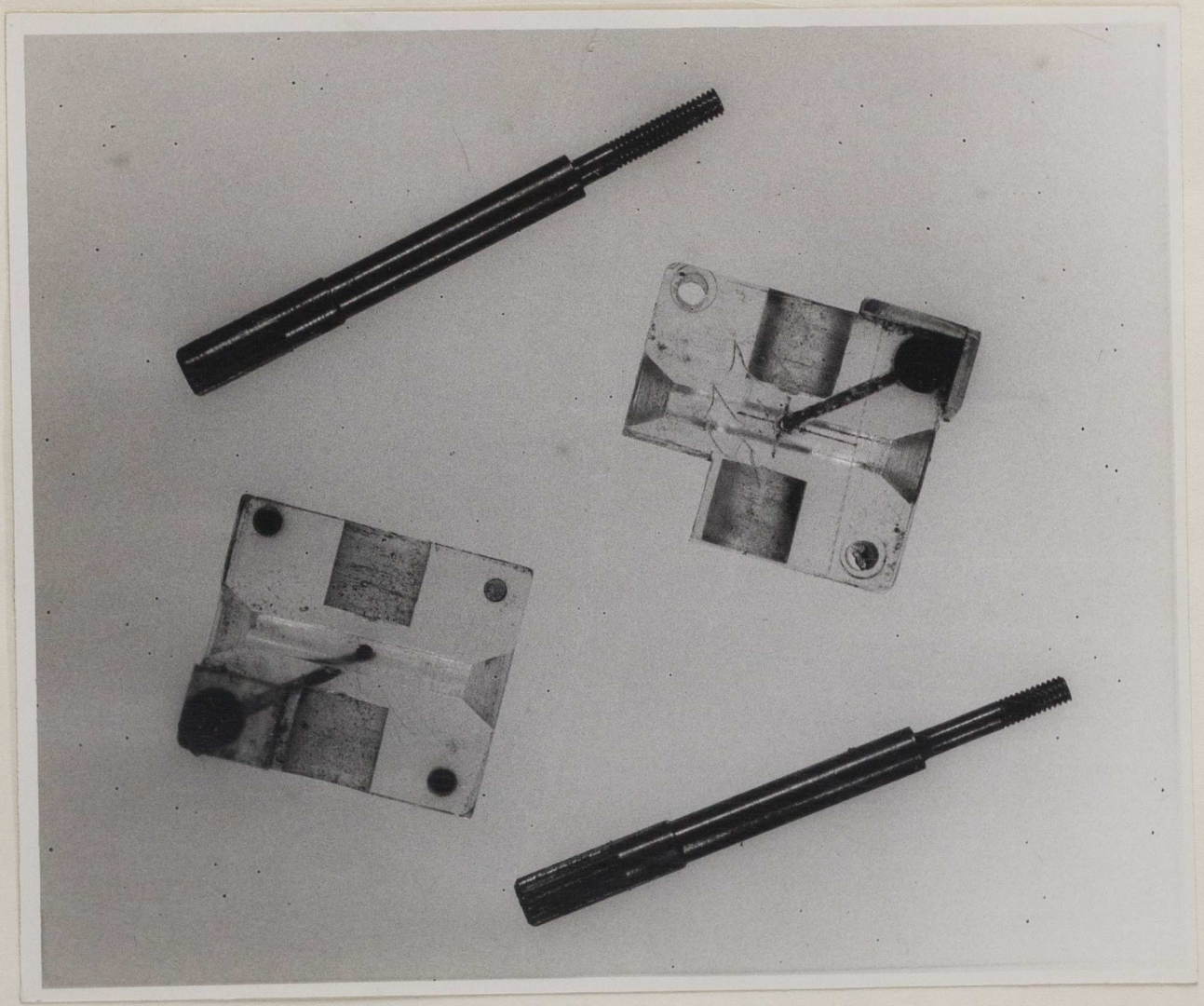


fig 15
for key see fig 13

The Arterial Cuff.

Special cuffs were designed to enclose the artery and prevent it pulsating. They also kept the artery, magnet and electrodes in constant relationship to each other. The cuffs were made of polystyrene - their shape can best be understood by reference to figs. (13,14,15). It will be seen that they are made in two halves which can be clamped with screws around the artery. The artery is fitted into the central channel. A set of cuffs were made with channel sizes from 2mm. diameter to 4mm. diameter in steps of 0.25mm. It was found that these fitted all the different sizes of carotid arteries in the dogs used in this work. A pair of recesses are provided to fit tightly about the magnet poles, and enable the axis of the artery to be kept at right angles to the magnet field. From the earlier discussion it will be remembered that the line joining the two points between which the potential difference is measured, the magnet poles and the direction of flow must be at right angles to each other. To achieve this and keep the cuff assembly as compact and as small as possible, holes were drilled in the two halves of the cuffs leading from the upper surface of the cuffs to the correct positions on the artery wall. The narrower part of the holes are filled with agar saline gel (1% Agar Agar in 0.9% NaCl solution) which conducts the E.M.F. to the electrodes which are thrust into the wider parts of the holes.

Recording Instrument.

If it be assumed that the internal diameter of a dog's

carotid artery is 0.3cm. diameter and that the mean blood velocity is that given by Lovatt Evans (1945) as about 40cms/sec. and the magnetic field strength is 2,000 gauss, substituting in equation (i) (page 11):-

$$P.D. = H.l.v.\ 10^{-8} \quad (i)$$

$$P.D. = 2{,}000. \times 0.3. \times 40. \times 10^{-8}$$

$$P.D. = 2.4 \times 10^{-4} \text{ volts or } 240 \text{ microvolts.}$$

From this it can be seen that the voltage expected from the electromagnetic flow meter is very small, hence a sensitive instrument is required.

In addition, if the variations in velocity during the pulse cycle are to be recorded, the frequency response of the instrument is of importance. If the frequency components of the velocity cycle are similar to those of the pressure cycle (and we have no reason to assume that they are not), an instrument capable of recording up to 150 cycles/sec. is needed. Wiggers, 1928, states that a suitable manometer to record all the pressure variations during the pulse cycle must be capable of recording frequencies up to 150 cycles/sec.; this figure is rather high - see the section on pressure recording, p. 31. As the flow meter was also to be used for measuring non-pulsatile flows, the recording instrument had to be a direct current reading instrument. Arising from these considerations it was decided that the only suitable instrument for this work was an electronic D.C. amplifier.

D.C. amplifiers are extremely difficult instruments to design since any variation in either a supply voltage or

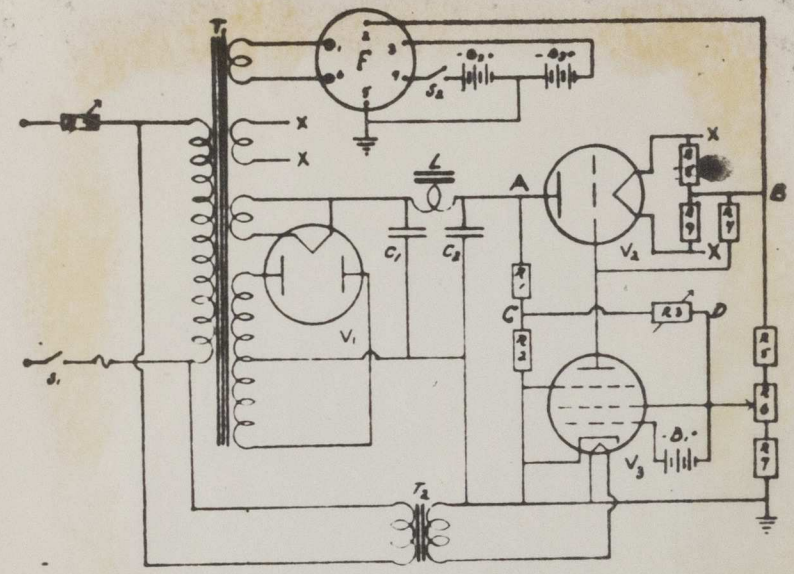


FIG. 2. Wiring diagram of regulated power supply showing devices used to maintain voltage of output constant despite changes in load and in line voltage.

Parts List

R_1 —1 megohm 1 watt	T_1 —power transformer (Thordarson T74 R28 or equivalent)
R_2 —75,000 ohm 1 watt	
R_3 —200,000 ohm variable	T_2 —6.3 volt transformer
R_4 —250,000 ohm 1 watt	V_1 —5U4-G tube
R_5 —150,000 ohm 2 watt	V_2 —2A3 tube
R_6 —20,000 ohm variable	V_3 —6J7 tube
R_7 —20,000 ohm 1 watt	B_1 —small 45 volt battery
R_8 R_9—20 ohm ½ watt	B_2 B_3—90 volt B batteries
R_{10} —10 ohm rheostat	F —female cable connector
C_1 C_2—8 microfarad 1000 volt oil filled condensers	S_1 —line switch
	S_2 —battery switch
L —10 henry 100 milliampere choke	

fig 17
Circuit of Stabilised H.T. Supply for Goodwin Amplifier.

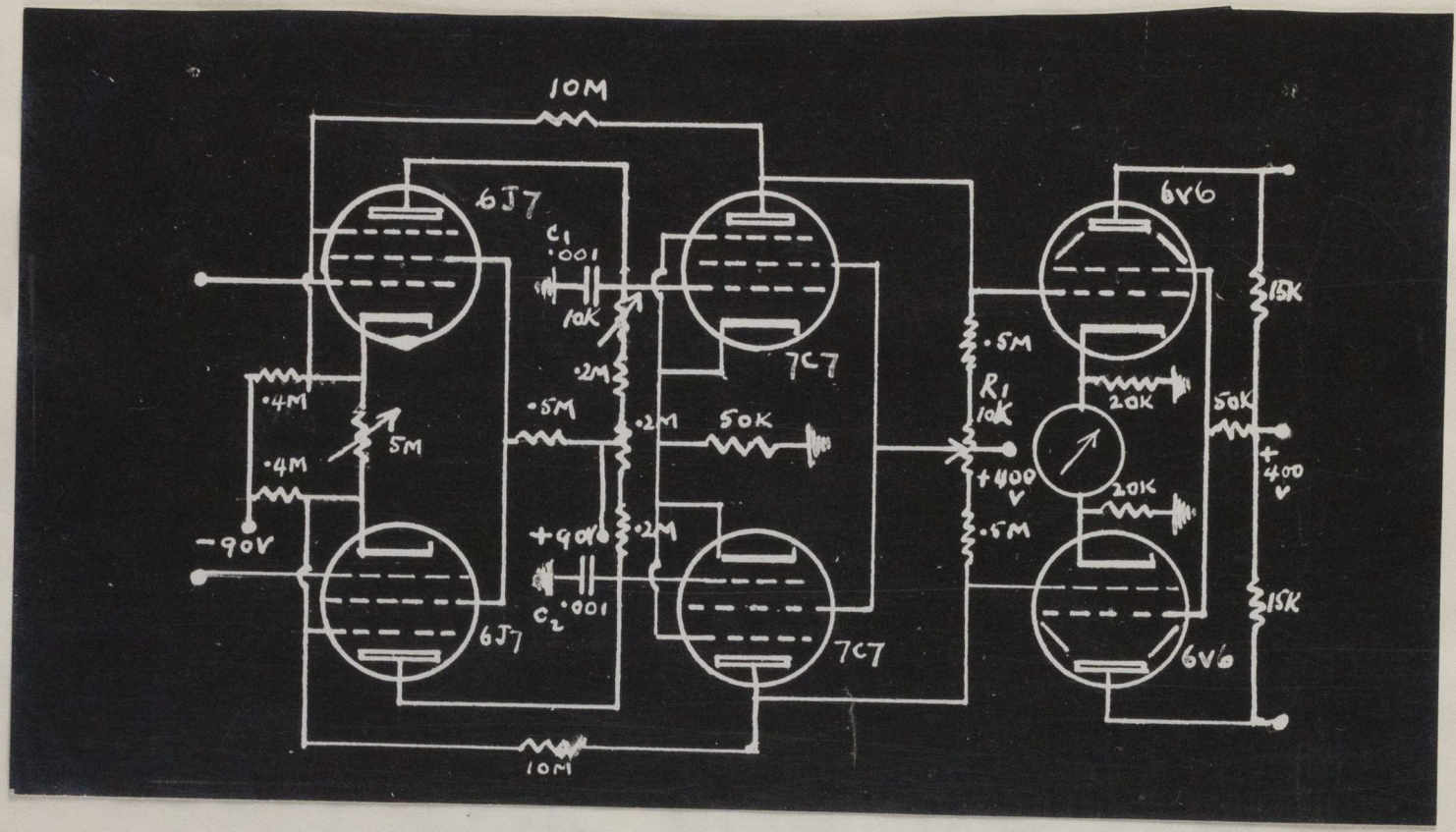


fig 17b
Goodwin amplifier circuit

component is amplified as a signal. A further difficulty with high gain amplifiers of this type is that interference from mains hum in the supplies to the amplifier or hum picked up by the input leads can swamp the signal; therefore special precautions must be taken to overcome this interference. In a paper by Jochim (1948) an amplifier is described which, he claims, is suitable for use with an electromagnetic flow recorder. This amplifier was built and was found to be a very fine D.C. amplifier with exceptional stability and a low noise level, but unfortunately its gain was not high enough for the signals from the flow recorder to be recorded satisfactorily on a Cathode Ray Tube. Further, its differentiation against mains hum on the input leads was poor and also its input impedence was low. From the experience gained from the Jochim amplifier it was decided that the amplifier described by Goodwin (1941) would be suitable as its gain was said to be better than 1×10^6 times, (figs.17A + 17B). In addition it had a specially designed stabilized power pack and as all the stages were push-pull with high value common cathode resistors, the differentiation against in-phase signals (i.e. mains hum) on both electrodes would be high.

In building the amplifier certain modifications and precautions were necessary. In the original circuit the input valves recommended were type 1620. These are special antimicrophonic versions of the 6J7; unfortunately these valves are not available in this country. The makers, R.C.A., state that the E.F. 37A can be substituted for the 1620. This was tried but

it was found that the performance was not as good as specially selected 6J7's, possibly 1620's are only selected 6J7's. The input valves were selected from a batch of fifty valves which were aged by running the heaters for seven days and then matched pairs of valves were selected with low noise characteristics. If the valves are not carefully matched it will be found impossible to balance the amplifier. The ageing procedure is advisable for the characteristics of valves change considerably over the first 100 hours of running and it is often found that new valves which have matched characteristics no longer match after ageing. In the original circuit no arrangement was made for balancing the second stage of the amplifier. Later the addition of R_1 (fig.17b) was found to be advantageous and when the grids of valves 2 and 3 were shorted together and the output then balanced on the meter, the performance of the amplifier was greatly improved. In the original circuit the heaters of the first two stages were run from accumulators and the last stage from heater windings on the mains transformer. It was found that the A.C. hum from the last stage heaters was picked up by the first stages and despite extensive screening could not be eliminated. To overcome hum, all the heaters were run from accumulators. Another difficulty then became apparent, for it was found that with even large capacity accumulators there was a steady drift due to the voltage of the accumulators falling on discharge. This problem was overcome by building a well smoothed six volt power pack which supplied the accumulator with the same amount of current as

the heaters consumed, thus keeping the accumulator fully charged. The accumulator's main purpose was to act as a ballast, and to absorb any variations in mains voltage reflected in the power pack output. A further modification that was found useful was to add the condensers $C_1 + C_2$, (fig 17B) for at low gain the amplifier tends to go into high frequency oscillation - these condensers prevent this happening.

With all these modifications it was found that if the two input electrodes were immersed in saline the amplifier was exceptionally stable for a D.C. amplifier. However, when the electrodes were in place in the cuff which was about an artery, the amplifier became unstable, and constant readjustment of balance became necessary. The stability was improved by covering the magnet with a rubber finger stall; a small hole in the rubber was sufficient to increase the instability. Further improvement was obtained by using for the earthing electrode a piece of silver about 1" square electrolytically coated with silver chloride, covered with cotton gauze damped with saline, and placed between the teeth and cheek of the dog. Despite these precautions the instability persisted, although to a lesser degree.

After a great deal of investigation it was discovered that the deterioration in performance was due to the grid current taken by the input valves of the amplifier. In the animal the resistance across the electrodes is constantly altering, due to variations in contact resistance and to drying of the tissues, (although this is prevented as much as possible by

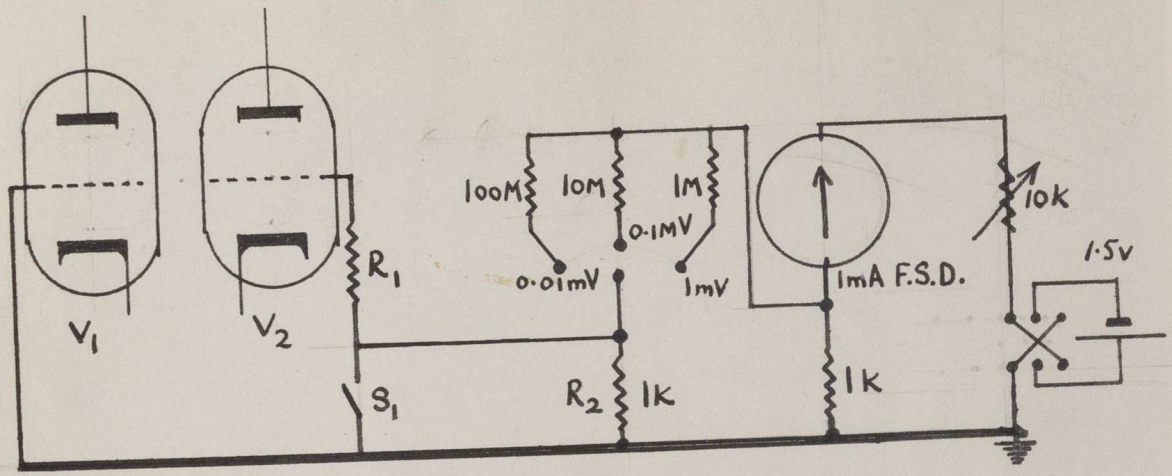


fig 18

To use the above circuit to measure the grid current of V_2, which is an input valve of the amplifier, R_1 is shorted out and the amplifier balanced. When R_1, which is usually about 10-100 M , is placed in circuit the amplifier will become unbalanced due to the grid current across the resistance. The rest of the circuit is used to apply a varying P.D. across R_2. The voltage across R_2 which is sufficient to balance the amplifier, therefore being equal to the voltage drop across R_1, is measured. By substituting the value of the applied P.D. + R_1 in Ohms Law the grid current can be calculated.

packing the wound with gauze packs soaked in saline). As the grid current is constant and is drawn across this varying resistance, the potential on the grids must vary correspondingly. This effect would be enhanced if a great difference existed between the grid current drawn by the two input valves. In view of this the grid current of the selected matched pairs of valves was measured by means of the circuit shown in Fig.18. It was found that the current drawn by the valves varied from about 10^{-7} amps. to 10^{-10} amps; fortunately a matched pair were discovered with a grid current of about 10^{-9} amperes. Using the low grid current pair of valves it was found that the stability of the amplifier improved in use. Various cathode follower input circuits were tried using M.E. 1400 electrometer valves or 954 acorn valves, but with all these circuits the internal instability was greater than that of the amplifier with the 6J7 input valves. All these modifications were therefore abandoned. Improvement might be achieved by using the Ferranti electrometer valves with common cathodes and a specified grid current of 10^{-15} amps; however, this has not yet been tried. It is now felt that the greatest degree of stability in the amplifier would be achieved by having some form of servomechanism which balanced the amplifier during the time the artery was clamped off for zero flow readings to be obtained.

The output of the amplifier is observed on a long persistance afterglow cathode ray tube with a suitable time base.

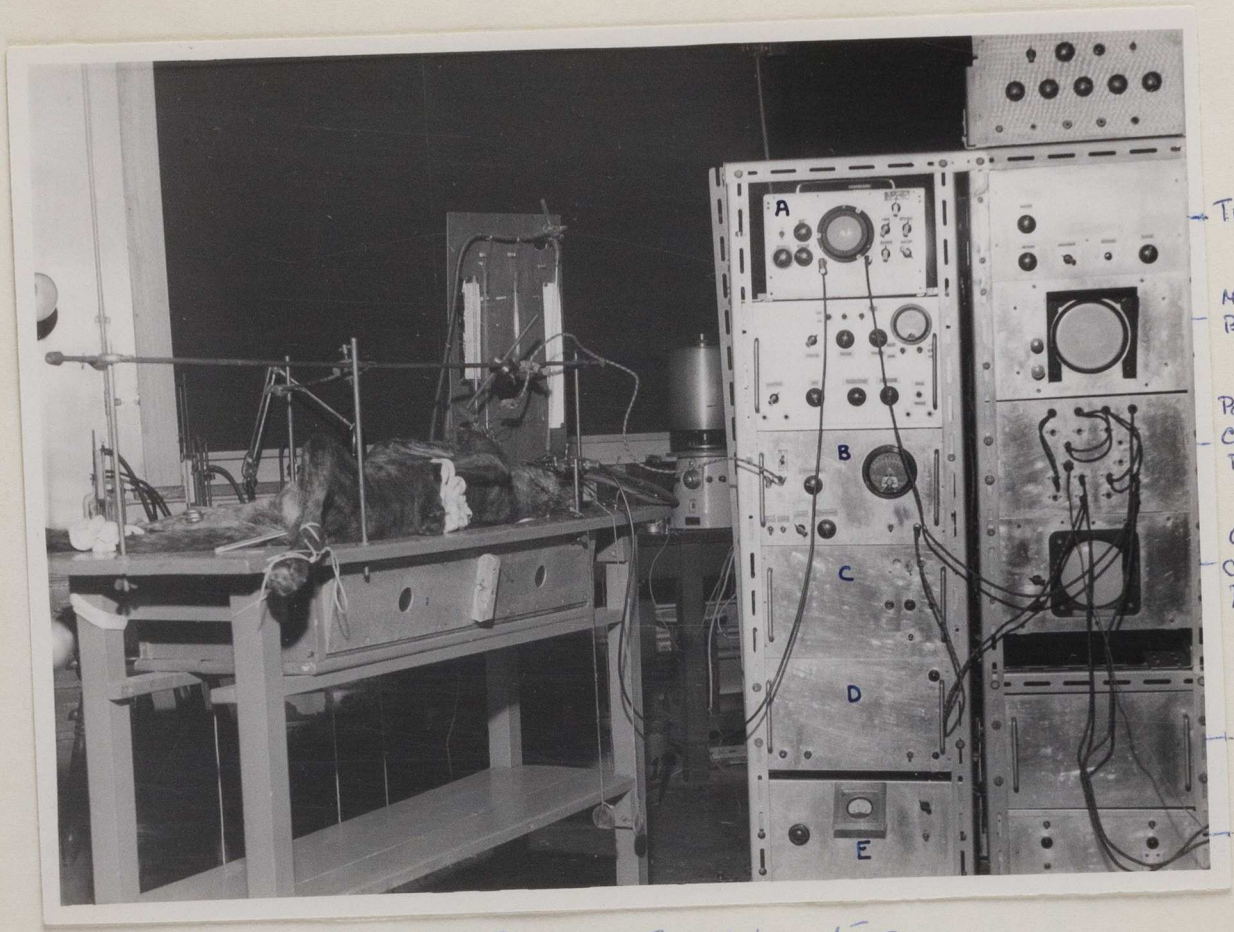
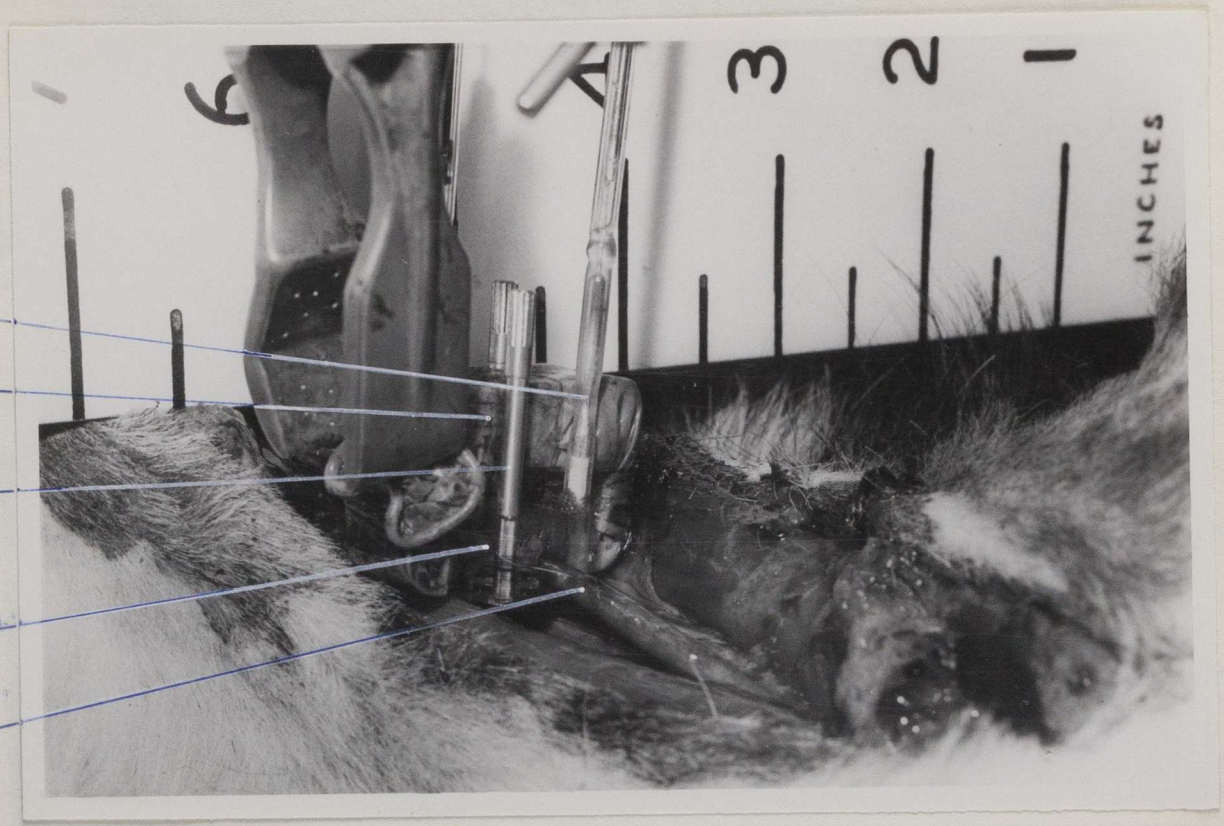
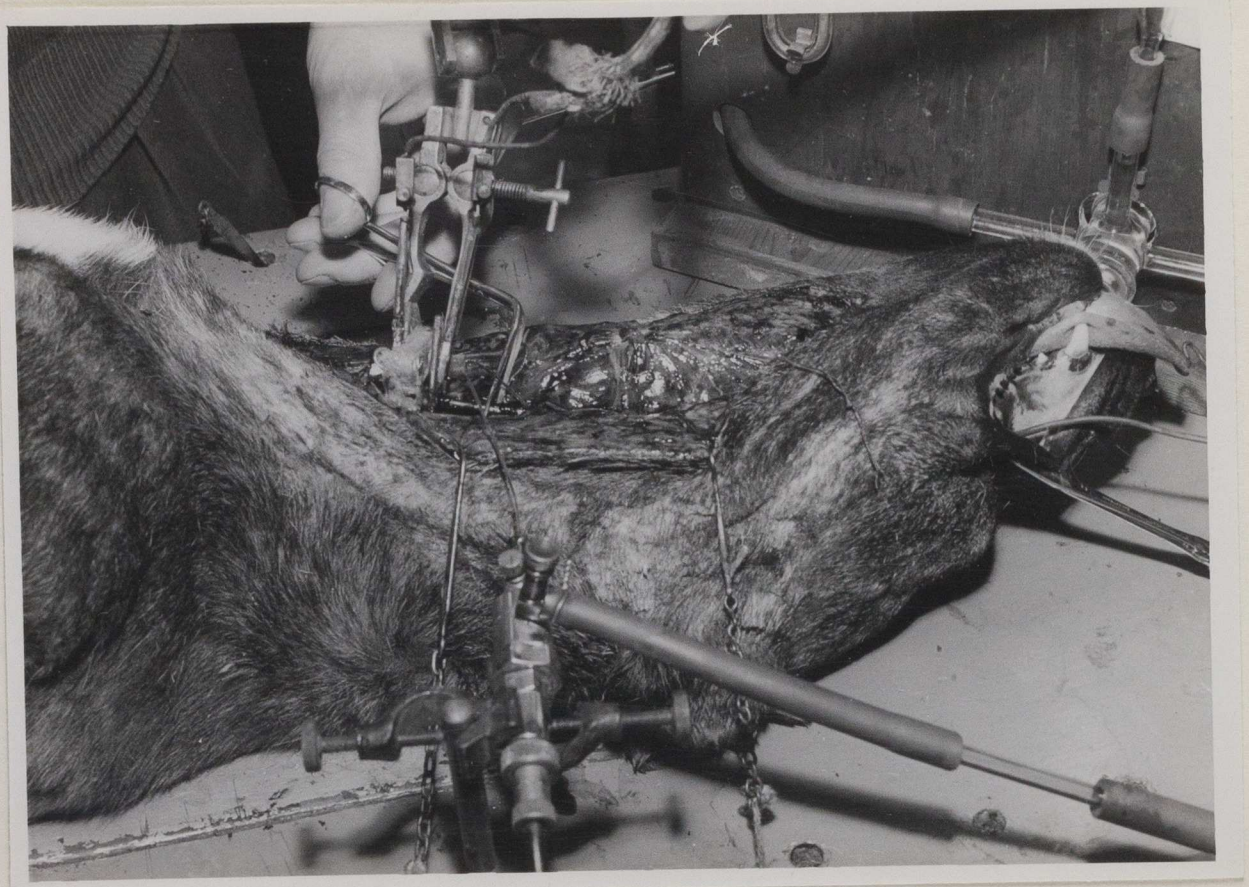


figure of apparatus.

A = Pressure Recording Unit
B = Goodwin Amplifier
C = Time marker Unit
D = Stabilized H.T. supply for B
E = Stabilized L.T. supply for B.



Recording head in situ



Clipping artery to obtain zero flow

Experimental

All the experiments described in this thesis were performed on dogs. The anaesthetic used was Nembutal (32mg./kg.). The flow meter cuff was applied to the carotid artery one to two centimetres below the superior thyroid artery. A cuff was selected from a number of cuffs; the cuff used was that with which arterial pulsations just failed to appear. Pulsation may be observed visually through the perspex cuff as a movement of air in and out between the artery and the cuff.

As the amplifier used exhibits a small degree of drift it is necessary to define zero flow at frequent intervals during any experiment. This is done by clipping the artery for a brief period distal to the cuff, thus giving a period of zero flow which is recorded by the flow meter. By joining successive regions of zero flow the zero level can be drawn in on the recorded traces.

Calibration was carried out on each dog at the end of a series of experiments. This was performed by tying into the artery a cannula distal to the cuff and perfusing known volumes of saline under pressure into the artery. This procedure was chosen for it ensures that the artery inside the cuff is distended by the arterial pressure, although it results in an irregular velocity curve due to the variations in the inflow rate caused by the difference between the arterial pressure and the perfusing pressure. The flow of saline or blood along the artery at the same rate induces the same E.M.F. and thus saline can be used in the calibration in place of blood (see

fig. 21). The calibration curve is made by measuring the area underneath the resultant velocity curves and plotting this against the volume of saline perfused. The areas of the curves are measured by tracing them on to millimetre squared graph paper and counting the enclosed squares; this is done to the nearest tenth of a square millimetre.

Pressure was recorded simultaneously with blood velocity, by means of a capacitance manometer, illustrated in fig.29 and discussed on page 33 et seq. The manometer was connected by polythene tubing inserted into the Superior Thyroid branch of the Carotid Artery examined. The polythene tubing did not project into the carotid artery or otherwise interfere mechanically with blood flow.

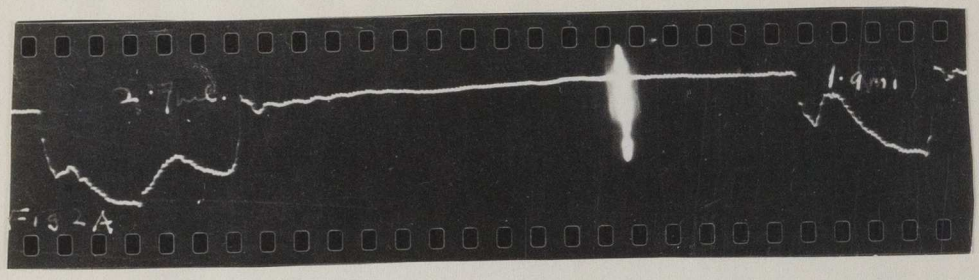


fig 19

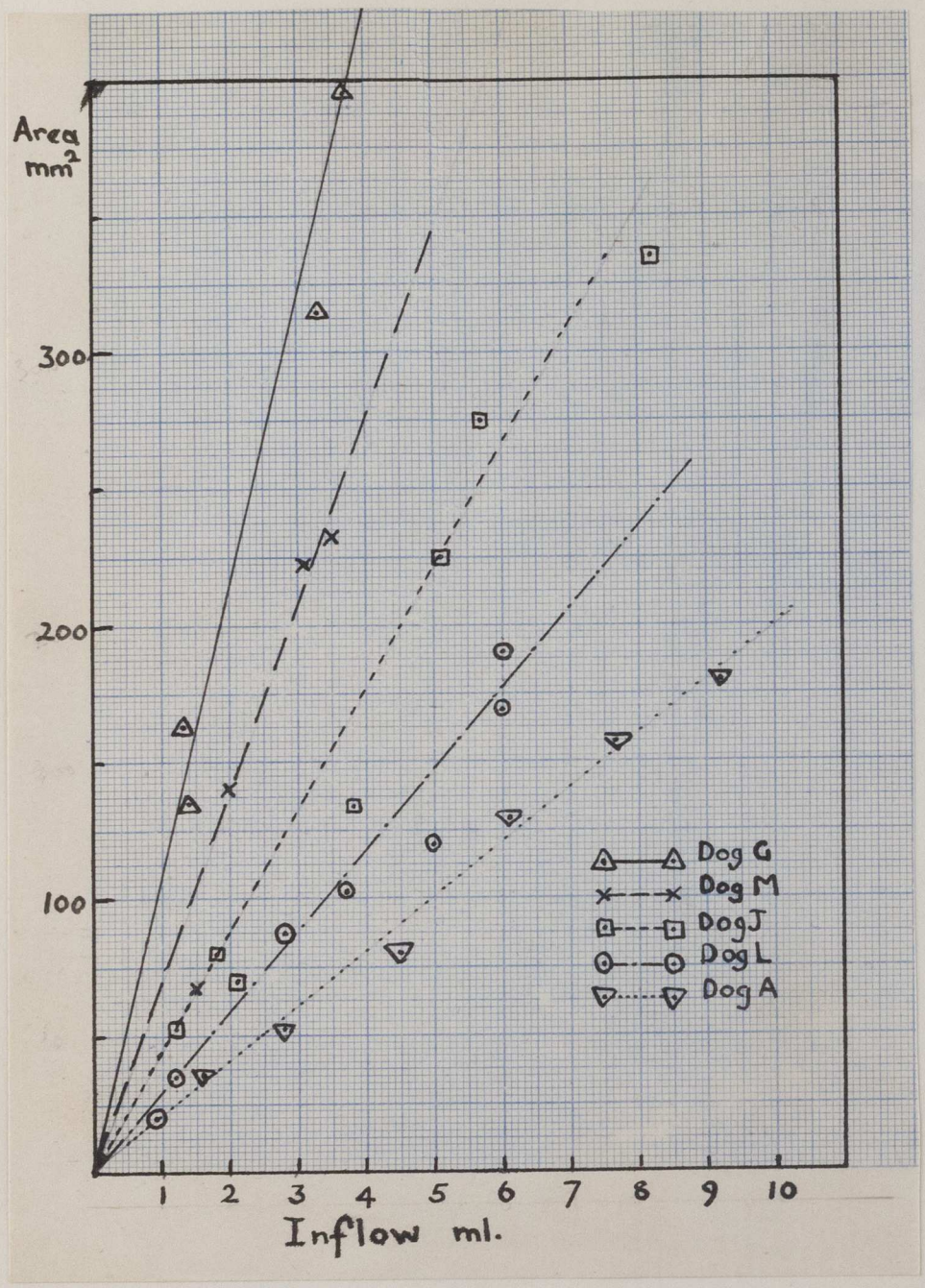

Area
mm²
300
200
100
1
2
3
4
5
6
7
8
9
10
Inflow ml.
Dog G
Dog M
Dog J
Dog L
Dog A

fig 20.

CRITIQUE OF THE ELECTROMAGNETIC FLOW METER

Frequency Response.

Theoretically the frequency response should be limited only by that of the recording instrument. In the case of records made with a cathode ray tube the limiting factor is the amplifier. The Goodwin amplifier had a frequency response linear up to about 7 Kc/sec. In the galvanometer unit the frequency response is limited by the galvanometer which is linear up to about 115 cycles/sec. However, in practice, the frequency may be determined in some way by the electrodes or the artery, and this must be tested *in vivo*. The ideal way is to examine the response of the system to a velocity wave of rapid onset as near to a square wave as possible. This is seen during calibration. If a typical calibration curve such as is shown in Fig. (19) is analysed it will be seen that the 'rise time' is very rapid. If the frequency components of the velocity pulse wave are the same as those of the pressure pulse wave, (and there is no reason to believe that they are not), this frequency is quite adequate to record the variations in velocity during the pulse wave.

Calibration.

From the formula, $E = Hlv.10^{-8}$, the calibration curve should be linear and should pass through the origin. Fig.(20) shows a series of calibration curves obtained in different

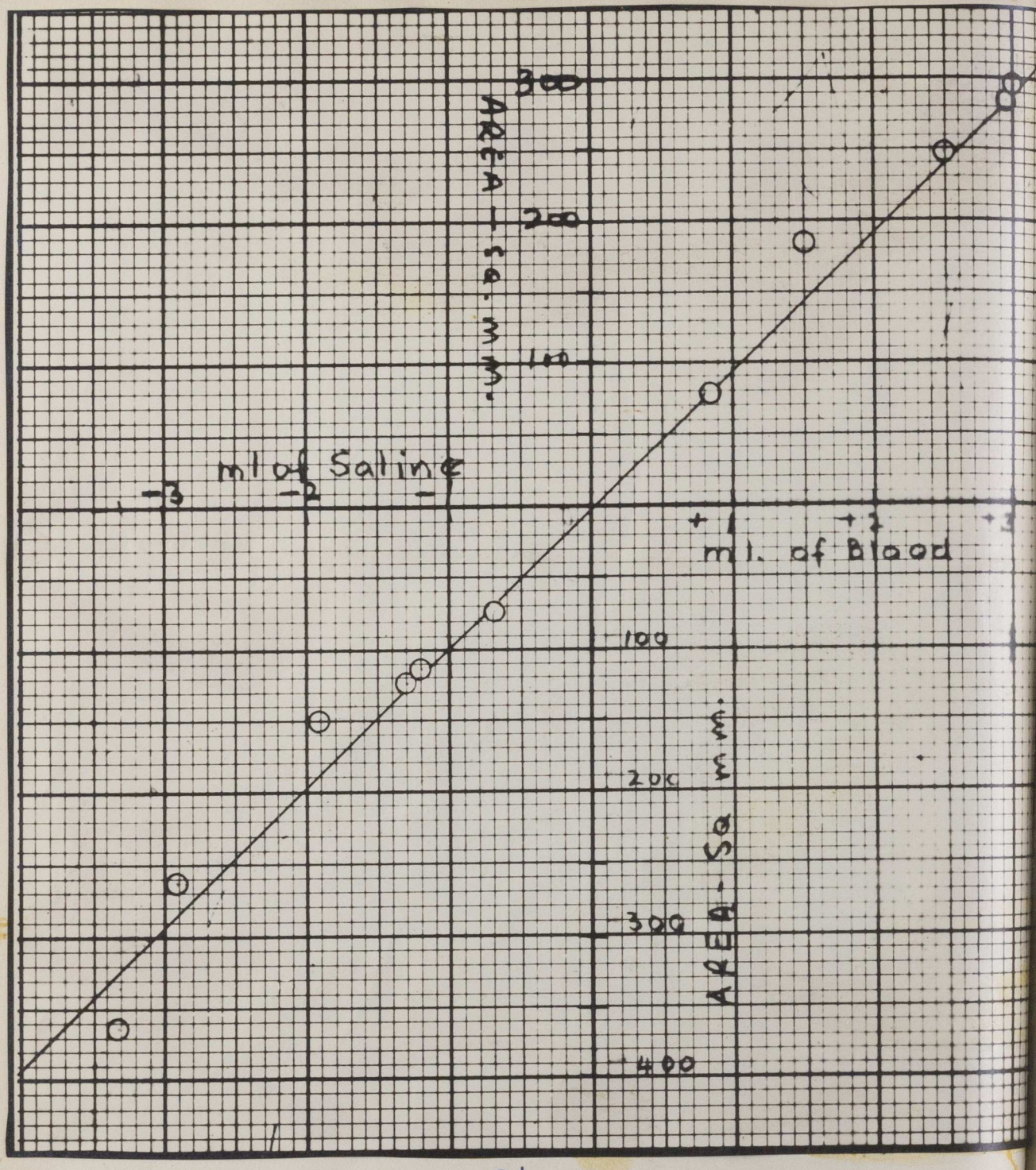

AREA - Sq. m.m.
300
200
100
-3
-2
ml of Saline
+1
+2
+3
ml. of Blood
100
200
300
400
AREA - Sq. m.m.

fig 21.

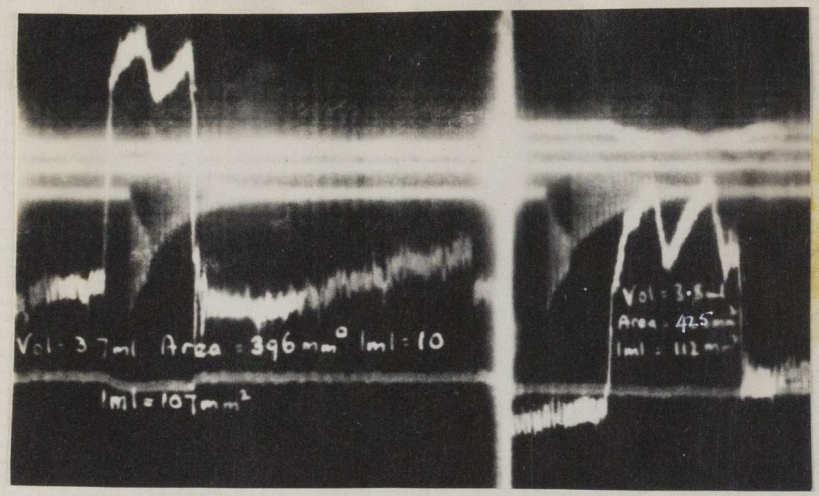

Vol: 3·7ml Area = 396 mm² 1ml: 10
1ml = 107 mm²
Vol: 3·8ml
Area: 42·5mm²
1ml: 11·2mm²

fig 22

dogs by the retrograde infusion of saline; it will be seen that they are all linear and that they pass through the origin. It might be objected that a calibration made with blood flowing in the normal direction gives a different calibration curve. Fig. (21) shows the results obtained from an experiment designed to test this. At first a calibration was made with saline in the normal way, then measured volumes of blood were allowed to escape from the cannula and this was recorded by the flow meter. It will be seen that the results obtained fit the straight line which passes through the origin.

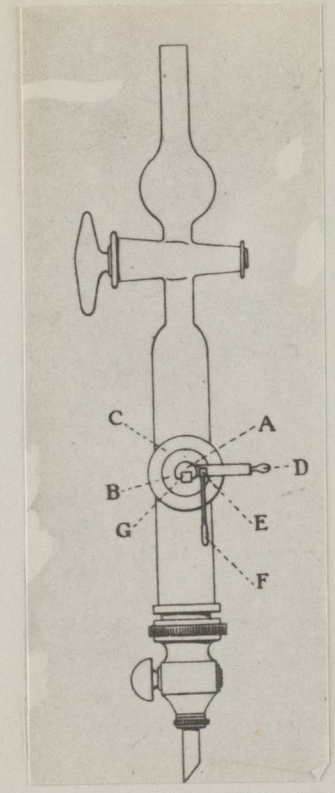
The possibility that velocity of flow might affect the calibration of the instrument was tested by infusing the same volume of saline at the different velocities. Fig.(22) shows the result and it will be seen that the areas are the same within the limits of experimental error.

Effect of resistive changes in the electrodes.

It is apparent from the calibration curve made when blood and saline were used that resistive changes have no effect on the calibration. To make doubly sure, records were taken first with Agar saline made from 0.9% NaCl solution in the cuff, and then with Agar saline made from 1.8% NaCl. in the cuff. The resistance across the electrodes in the first case was 10.3K ohms. and in the second 8.6K ohms. No difference could be detected between the records.

Pressure Recording.

Wiggers (1928) states that "The requirements of a good manometer are: (a) that it inscribe a curve which has a



A= Rubber Membrane

G = Mirror Cemented on Membrane.

fig 23

sufficient amplitude to show changes in gradient and finer vibrations, (b) that it respond without measurable lag, and (c) that it reproduce the pressure variations correctly as regards amplitude and phasic relations". To achieve these requirements a manometer must have a high resonant frequency. Frank (1908) showed that the resonant frequency "N" is determined by the following formula:-

$$\frac{1}{N} = 2\pi \sqrt{\frac{M^1}{E^1}}$$

where E^1 equals the volume displacement into the manometer per unit rise in pressure, and M^1 equals the effective mass of the manometer; this is proportional to the length and cross-sectional area of the manometer system, i.e. L/A. Therefore, to achieve a high resonant frequency, M^1 must be as small as possible and E^1 as large as possible.

To fulfil these conditions, Wiggers designed his rubber membrane manometer which was short and of great cross-sectional area, therefore having a small M^1.

It recorded on photographic paper by the deflection of a beam of light shone onto a small mirror cemented to the edge of the membrane. (Fig.23). Hamilton devised a further refinement of the Wiggers manometer by replacing the rubber membrane by a metal membrane made of either phosphor bronze or beryllium copper, thereby giving a high E^1. The advantage of the metal membranes was that they were more stable and had a higher

frequency response. The disadvantage of the Hamilton manometer was that since the movement of the membrane was much smaller than in the Wiggers type, the deflection of the light-lever was proportionately smaller. This could be overcome by making the light-lever longer, but an apparatus with a light-lever of five metres is extremely difficult to manage; even then the results have to be studies with the aid of a dissection microscope.

However, a most ingenious method of overcoming the disadvantages of the Hamilton type manometer whilst still retaining all its advantages, is to record the deflections of the membrane electrically. The method uses the metal membrane as one plate of a condenser, and an insulated electrode placed very close to the membrane as the other plate, the two together acting as a condenser. When the pressure applied to membrane increases, it bulges and approaches closer to the insulated plate, thereby increasing the capacity of the condenser. The rise in capacity of the condenser is proportionate to the rise in pressure. A full analysis of the condenser manometer is given by Hanson (1947). The capacitance change in these manometers is very small but, by the use of suitable electronic apparatus, the changes can be detected. Suitable apparatus is described later (p.36).

The manometer used in this work was a commercial manometer manufactured by Southern Instruments Ltd. This manometer was one of a batch made by this firm, and it was the only one of the batch found to be suitable for recording arterial blood pressure.

Wiggers (1928) gives some figures for the performance of a manometer which he considers suitable for recording faithfully arterial blood pressure changes. These are:-

Sensitivity. This should be in the region of 1mm. deflection of the light spot to 5mm. of mercury pressure change with a camera speed of 8 cms. per sec. With an average pulse pressure of 60mm.Hg. and a heart rate of 60/min. this gives a tracing which would fit almost into a square. This sensitivity may be easily obtained with a condenser manometer by increasing the gain of the detecting device, but for use with multichannel recording it would need very wide photographic paper to prevent overlapping and in experiments lasting for hours the consumption of paper would be very high. It was found in practice that a sensitivity of approximately 0.75 cms. deflection per cm. of mercury of pressure with a paper speed of 1.5 cms./sec. was quite adequate to show all the pressure changes and the amount of paper used was not inconveniently great.

Frequency response. Wiggers made a harmonic analysis of an intraventricular pressure tracing obtained with his manometer, and found that harmonics up to the 10th harmonic were present. He states therefore that a manometer should be capable of recording a frequency ten times greater than the fundamental. To do this faithfully it should have a natural frequency four to five times as great as the tenth harmonic. The average heart rate of a dog is about one hundred beats per minute, so that the fundamental frequency of the pressure curve is approx.

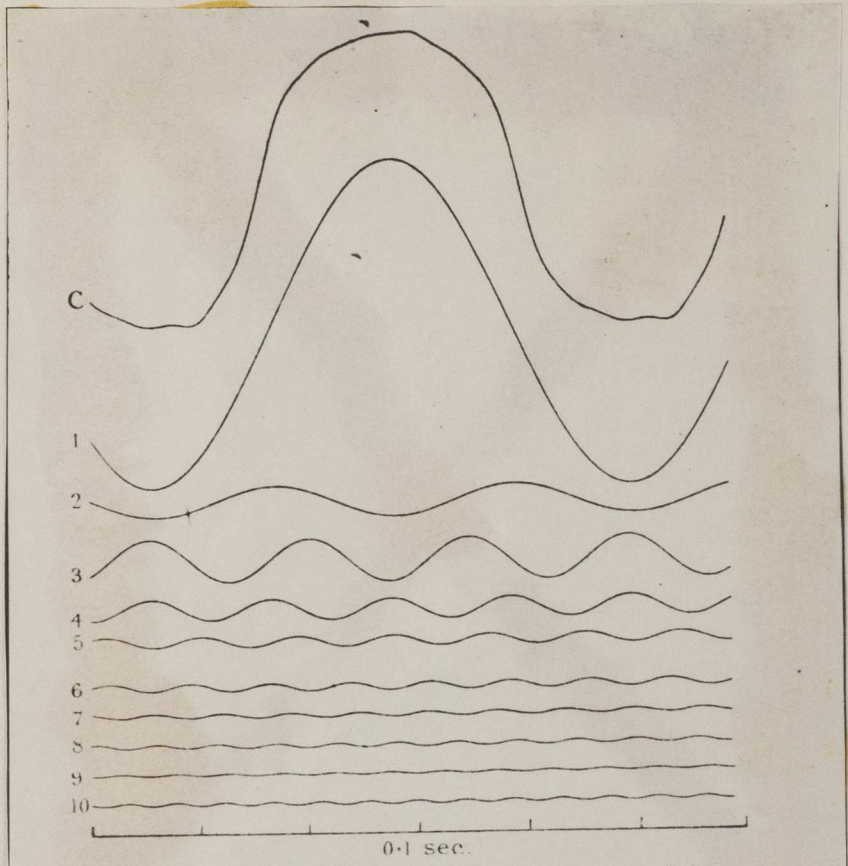
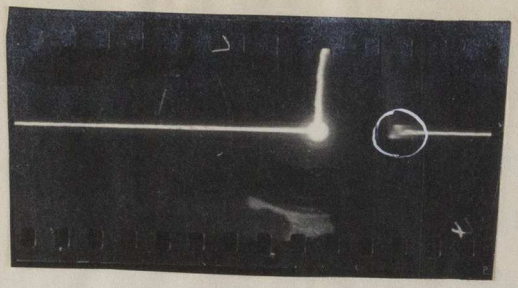


FIG. 1.—Resolution of a normal intraventricular pressure curve (*C*) into ten components (1-10) by means of an Henrici harmonic analyser.

Amplitudes of successive components in millimetres on original curves: 137·2, 12·6, 18·8, 8·5, 4·9, 3·4, 1·5, 2·3, 0·8, 1·6. Phases of successive components, 293°, 311°, 105°, 190°, 22°, 64°, 230°, 269°, 144°, 134°. (Exp. C388-I.)

fig 24

1.6 cycles/second, hence the tenth harmonic is 16 cycles per sec. and a frequency four or five times as great is 64-80 cycles per sec. These contentions cannot be so easily accepted, for the analysed tracing is from Wiggers own manometer, and we do not know whether the tenth harmonic is present in the ventricle or whether it is added by the manometer. Indeed, if Wigger's fig.1. (Fig.24) is examined it will be seen that beyond the fifth harmonic the amplitude of the harmonics are slight and it is doubtful whether they have a serious effect on the form of the pressure wave. A further difficulty in using high frequency response manometers, and one which, it is felt, is especially relevant to Hamilton manometers, is that they may respond to unphysiological changes in pressure. For example, if a needle is introduced into the blood stream, turbulence is set up about the needle tip; the turbulence will give rise to high frequency changes in pressure that may well be recorded by the manometer. It is thought that some of the high frequency vibrations seen in Hamilton's tracings are due to this cause. It is therefore believed that a manometer sufficiently sensitive to record the fifth harmonic is quite adequate, and, if a manometer of high frequency response is used, great caution should be observed in stating the probable cause of any high frequency oscillation present in the pressure curve. Taking the above figures, the fifth harmonic represents a frequency of 8 cycles/sec. and the desirable manometer frequency would be around 40 cycles/sec. The natural frequency of a manometer may be determined by subjecting the manometer to a very rapid rise



paper speed = 11.5 cm/sec
frequency = 76.5 cyc/sec
λ = 0.2217
λ = 0.706

fig 25 cf. fig 27.

The figures showing the frequency responses are reproduced from the original negatives. The measurements were made on the negatives using a measuring microscope. For clarity the resonant vibrations have been ringed in white. Owing to the limitations of the pressure recording instrument and camera it was not possible to obtain records of greater amplitude or time spread.

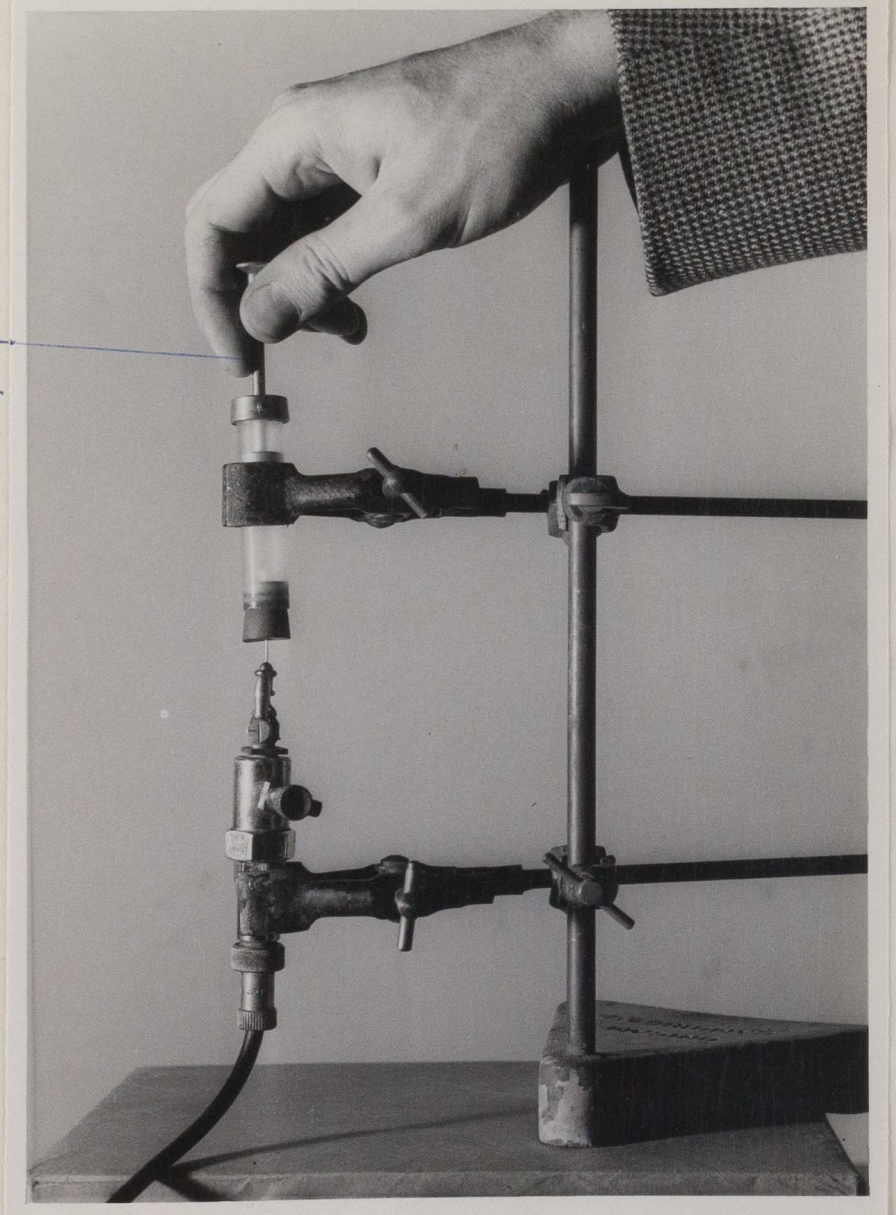
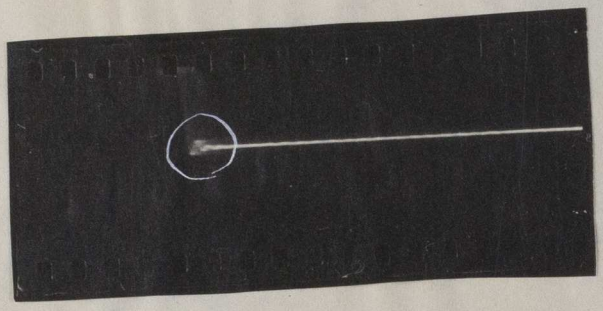


fig 26



paper speed 11.5 cm/sec
frequency = 115 cyc/sec.

fig 27
C.f. fig 25

or fall in pressure, as near to a square wave impact as possible, and then determining the frequency of the vibration that the manometer executes. Fig.(25) shows such vibrations for the manometer used in these experiments.

The square wave impact was obtained by using the device described by Hansen (1947). This consists of a 10 ml. hypodermic syringe with the nozzle removed and replaced by a rubber bung through which the tube to the manometer passes; a fine hole is drilled through the centre of the plunger and a side hole drilled into this in the stem of the plunger (Fig.26). To operate this device the plunger is pushed into the syringe and the air allowed to escape through the hole in the plunger. Then a finger is placed over the side hole and the plunger is rapidly withdrawn. As the plunger is withdrawn the pressure in the syringe falls; when the plunger leaves the barrel of the syringe the pressure is rapidly restored to atmospheric pressure, giving a good square wave impact to the manometer. From the figure it can be seen that the resonant frequency of the manometer and its system is 76.5 cycles per sec. It is important when measuring the resonant frequency of a manometer to include any tubing which is used to connect the manometer to the artery in the test. Fig.(27) emphasizes this point, for without the polythene tubing used in the experiments the resonant frequency of the manometer is 115 cycles per second.

Damping. This is of importance in a manometer for, if the system is underdamped the manometer will tend to overshoot or,

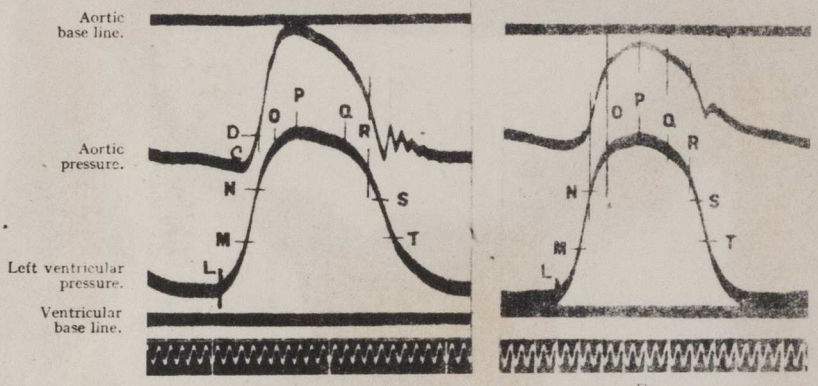


FIG. 14.—Normal left intraventricular and aortic pressures (Type I.).

Observe correspondence of pressure summits in the two pressure pulses. Letters indicate changes in gradients of ventricular pressure curve and serve to demarcate dynamic phases of contraction: *L–N*, isometric contraction phase; *N–R*, ejection phase sub-divided into minimum ejection (*N–Q*), maximum ejection (*O–P*), and reduced ejection (*P–R*).

L–M, entrant phase of fractionate contraction; *M–N*, unified isometric fractionate contractions; *Q–R*, exit phase of fractionate contractions; *R–S*, protodiastole; *S–T*, isometric relaxation. Time, 0·02 second. (A, Exp. C361–XII., *b*; B, Exp. C374–I., *b*.)

fig 28

if overdamped will undershoot and in either case will give spurious recordings. According to Wiggers, damping is relatively less important if the resonant frequency is well in excess of the maximum frequency it is desired to record, but if the frequencies are similar the system should be nearly aperiodic having a damping factor of almost 1.0; it is said that a damping co-efficient of about 0.7 is ideal. This statement must be considered more fully.

If the pressure which the manometer is recording changes rapidly it is likely to set the manometer into resonance (this does not mean that a high frequency is actually present for the turbulence would be sufficient to cause the resonant vibrations). Unless the manometer is damped adequately spurious pressure vibrations are likely to be recorded. Some of Wiggers figures seem to show this phenomenon, for example, his Fig.14 (reproduced as Fig.28). In both aortic pressure curves resonance vibrations appear to be present at R. The frequency of these vibrations is about 58 cycles/sec. which is slower than the frequency of the manometers that Wiggers says he uses. Further, Hansen (1947), using an adequately damped manometer with a higher frequency response than Wiggers, shows much smoother pressure curves. It is believed therefore that all manometers should be critically damped whatever the resonant frequency.

The damping coefficient can be determined from the curves inscribed during the experiment to determine the resonant frequency. In the curve of Fig.25 it will be seen that the

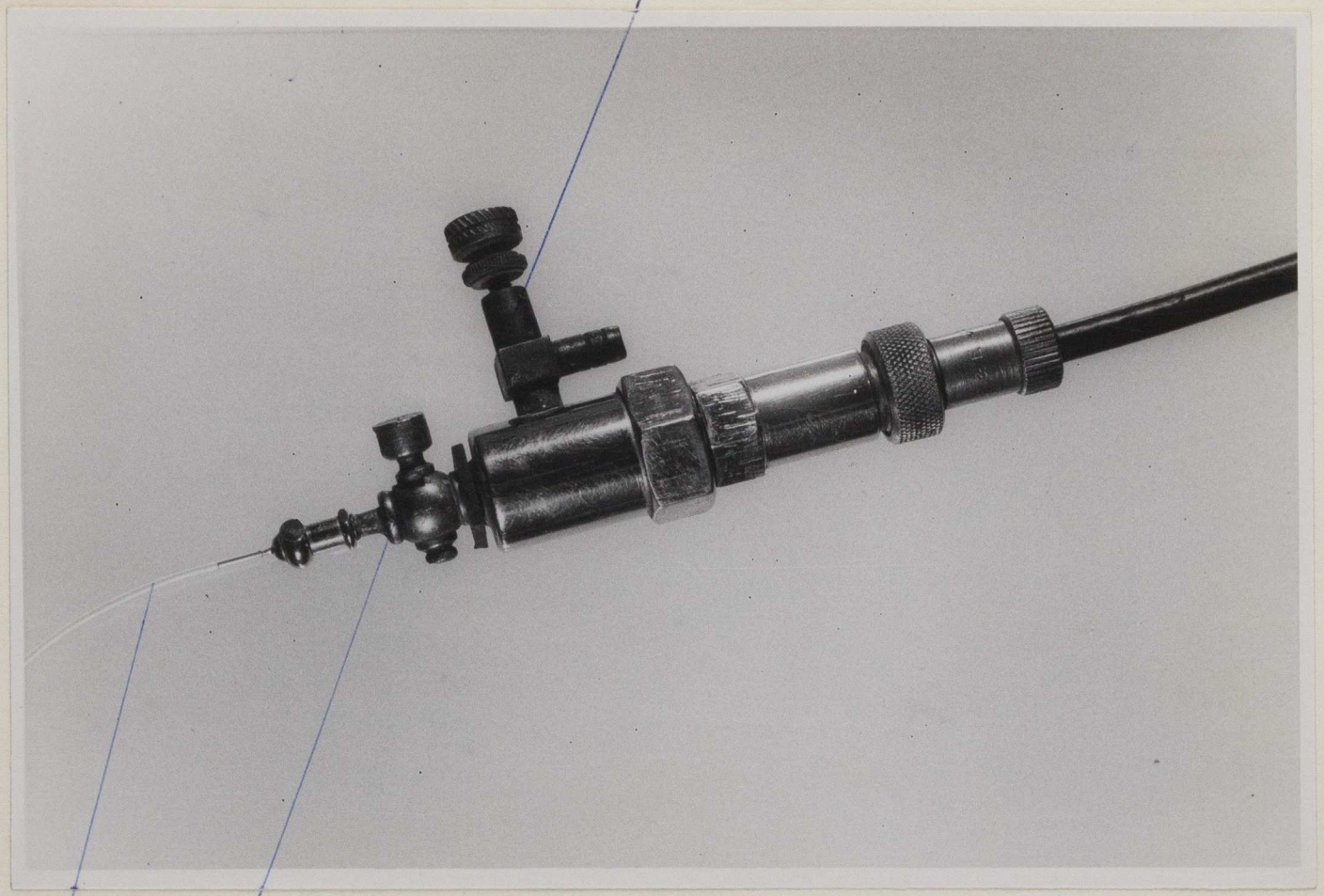


fig 29

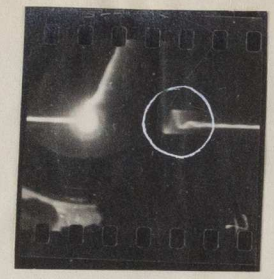
Condenser Manometer

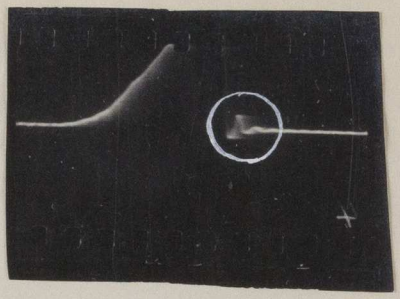
successive vibrations decrease in amplitude, the rate of decrease being determined by the friction or damping in the system. The ratio by which successive single vibrations decrease is the "decrement" and its natural logarithm is the "logarithmic decrement". The damping coefficient is determined from the equation:-

$$D = \frac{10\ \Lambda}{\sqrt{\pi^2 + \Lambda^2}}$$

where D is the damping coefficient and Λ is the logarithmic decrement.

Fig (29) shows a picture of the condenser manometer; it will be seen that it has a three way tap and a needle valve attached to it. In practice it has been found well nigh impossible to make leak-tight taps and connections for the manometer, so blood leaks back into the manometer and clots, and air may also leak in. Air must on no account be allowed in the manometer since it will reduce the elasticity of the manometer system, and hence seriously reduce the frequency response. The needle valve enables one to overcome these difficulties; to it a supply of heparinized saline from a pressure bottle is connected, and from this the manometer can be filled. When the manometer is filled the pressure in the bottle is increased to about 250mm.Hg., i.e., well above the systolic pressure of a dog, and the needle valve is opened so that about one or two drops of saline per minute are delivered. This keeps the manometer full of saline making





tap open
frequency = 46 cyc/sec

tap closed
frequency = 46 cyc/sec

10 cm of polythene tubing attached to manometer.

fig 30

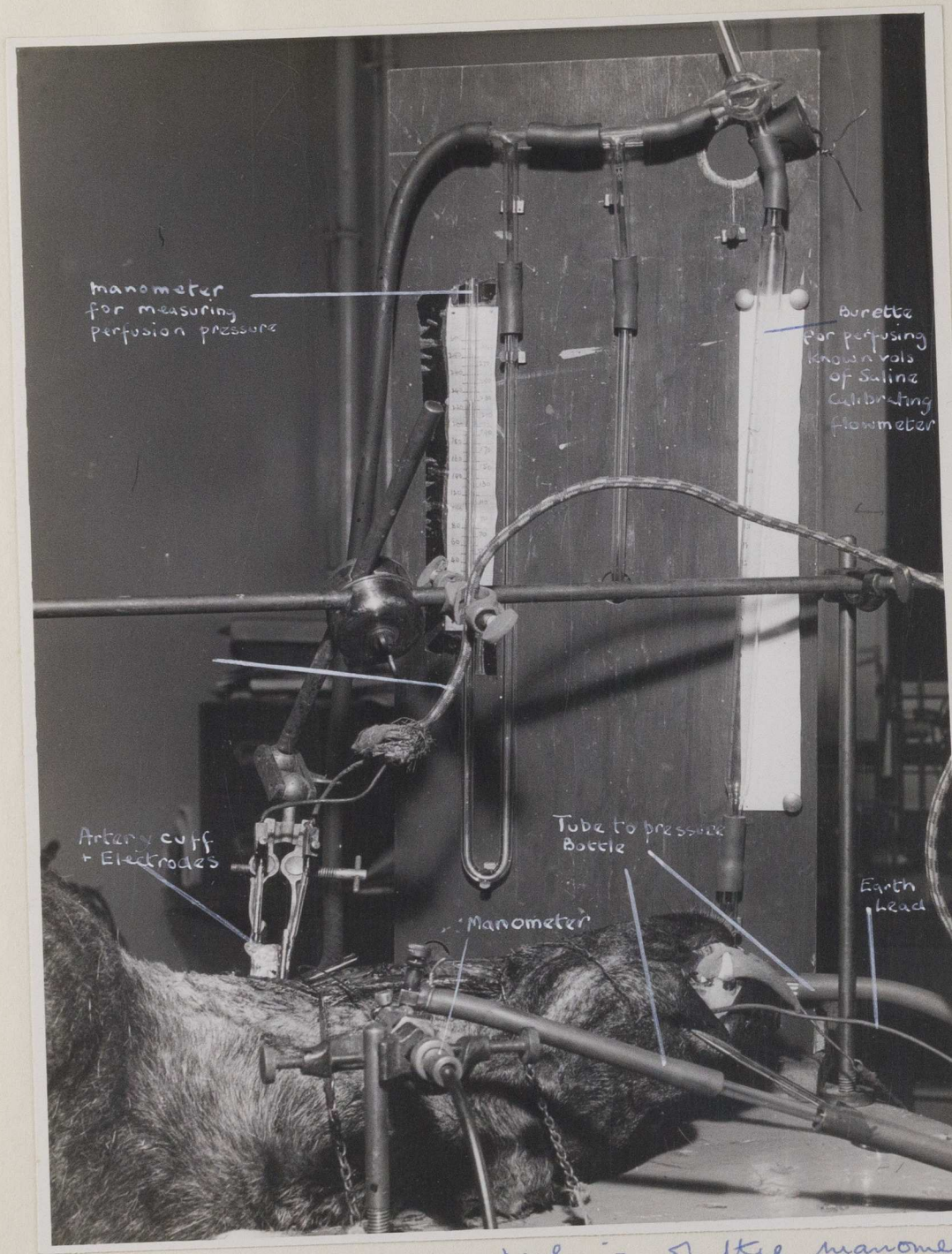


fig Showing pressure perfusion of the manometer.

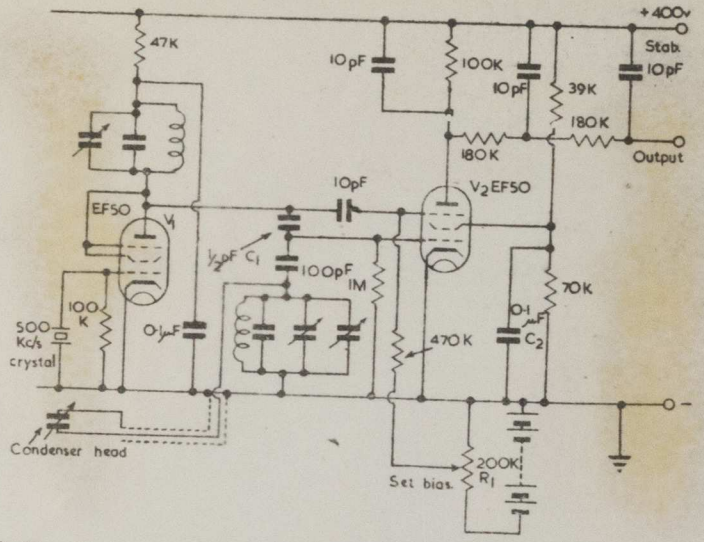


Fig. 53.—Frequency modulation phase discriminator circuit (500 kc/s) for registration of small changes in capacitance.

fig 31

up for any leaks at joints. Because the frictional resistance is so high across the tap, no difference in frequency response is apparent. An experiment to test this is illustrated in Fig. (30). The curve shows the response of the manometer to a square wave impact with and without the needle valve drip. The resonant frequency and the damping are identical.

The three way tap is useful for it enables the manometer to be closed off from the artery and calibration can be carried out by opening the needle valve and measuring the pressure in the pressure bottle supplying saline. Also intra-arterial injections can be made via the side arm of the tap. The manometer is connected to the artery by a piece of 0.5mm. diameter bore polythene tubing attached to a No.12 hypodermic needle. Polythene tubing has two advantages; in the first place, it may be cut to a length which, under test, provides the correct damping, and, secondly, the passage of blood towards the manometer may be seen and the needle valve adjusted to prevent this.

Detector Circuit. The electronic circuit used to detect capacitance changes in the manometer is shown in Fig.(31). This circuit is described by Dickenson, 1950, and depends on the principle of phase shift. V_1 of the circuit acts as a reference oscillator, and oscillations from it are applied to the suppressor grid and control grid of V_2. Variations in the condenser manometer alter the phase of the signal applied to the control grid of V_2. The output on the anode of V_2

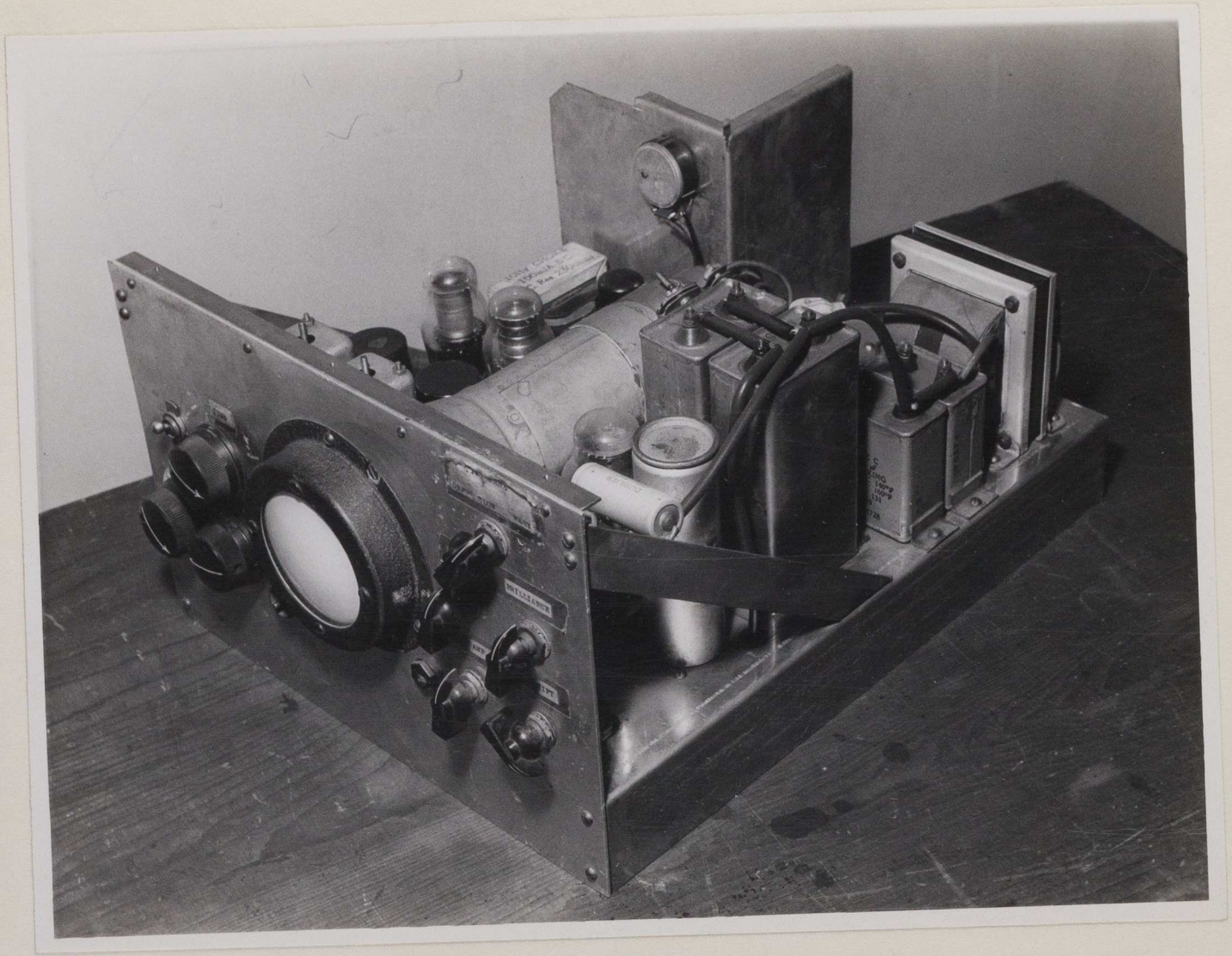


fig 32
Pressure Recording Unit.

is a measure of the phase difference between the two oscillations. The circuit with its power supplies was built into a single unit with its own monitor cathode ray tube and time base, and an outlet was provided to supply the photographic recording unit.(Fig.32).

Photographic Recording Unit. In the early part of this work before the pressure recording unit was developed the flow tracings were recorded from a VCR 97 cathode ray tube using a Cossor type moving film camera loaded with Ilford fast orthochromatic film. Time marking was arranged by applying a pulse from a thyratron, driven by a clockwork contact unit which closed every $\frac{1}{2}$ second, to the grid of the cathode ray tube and blanking out the beam for about 0.05 secs.

Later it was necessary to record flow, pressure, integrator output, time and signals simultaneously. Great difficulty was experienced in obtaining suitable equipment. A unit was made using four one inch cathode ray tubes and trying to photograph them simultaneously, but they could not all be focussed simultaneously with the Cossor camera and further, four traces on 35mm. film meant having very small traces to avoid overlapping. The commercially made pen writers were very expensive, delicate and their frequency response was also rather low for the work in hand. Finally, the Admiralty Research Laboratory kindly loaned us a twelve channel galvanometer. The galvanometer was designed for torpedo research, and made up into a very compact unit containing a camera and motor to fit in a

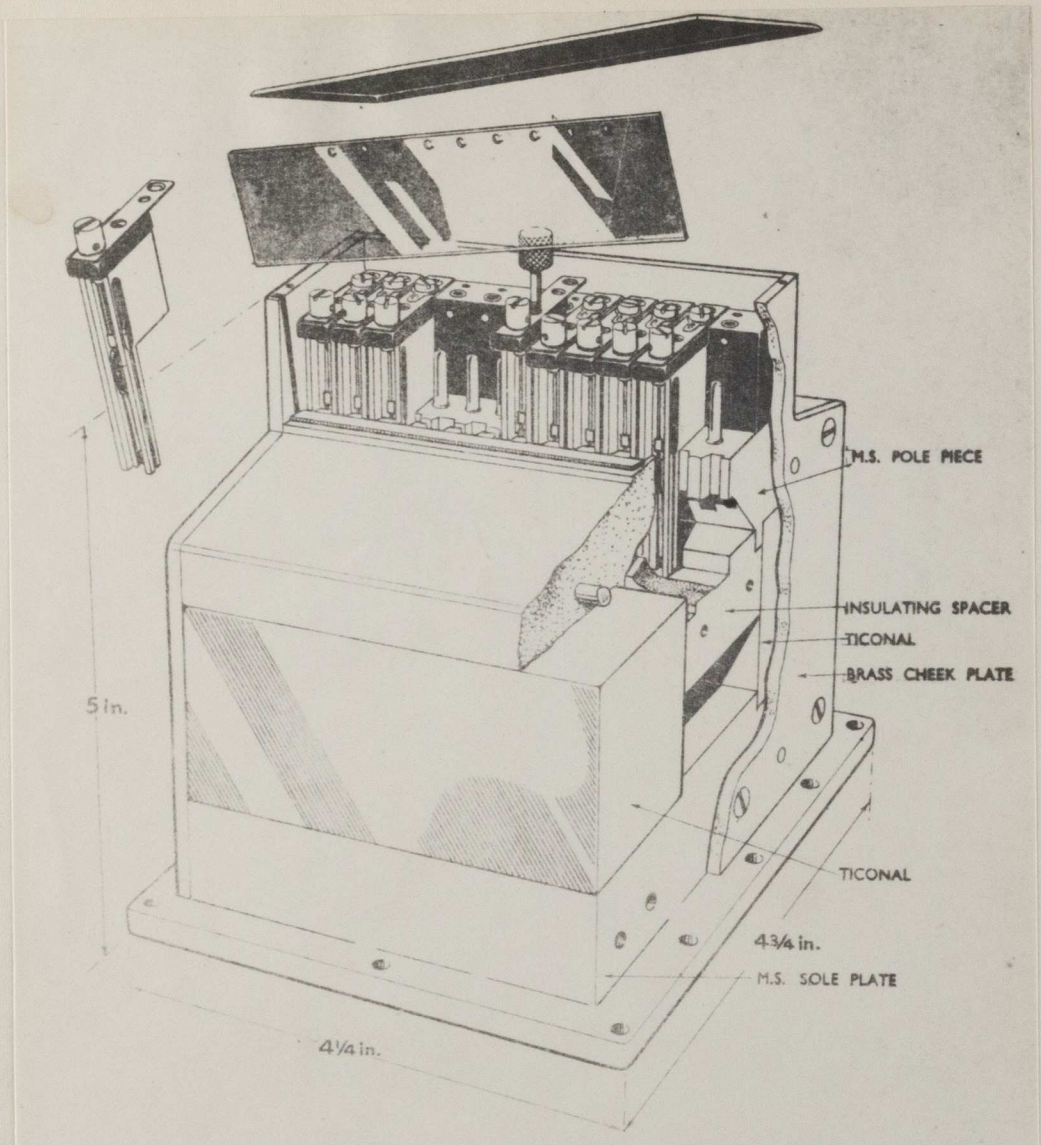


Fig. 1 GALVANOMETER SHOWING ONE ELEMENT PARTIALLY REMOVED BY EXTRACTING TOOL

fig 33

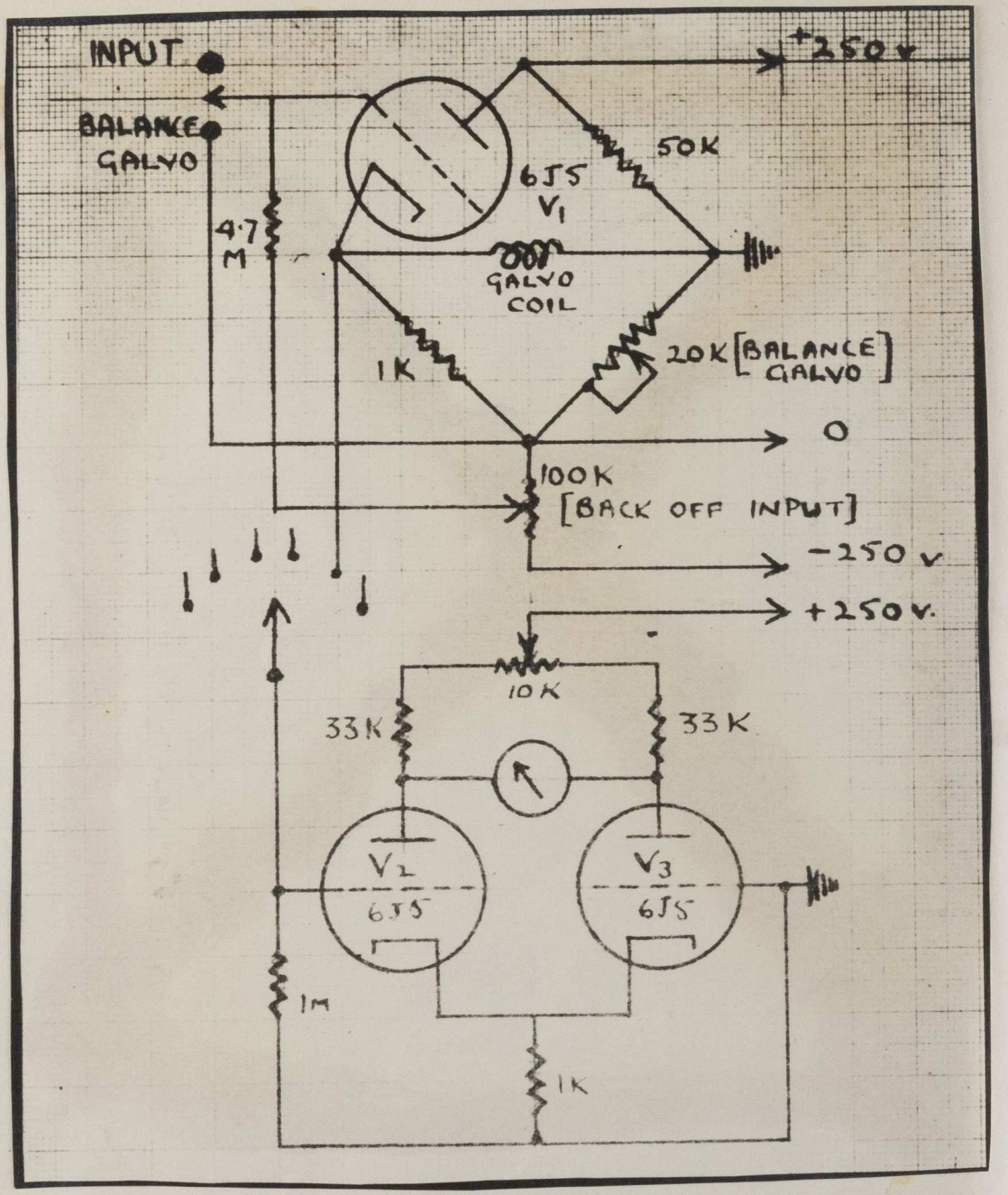


fig 34
Circuit of Galvanometer Control Unit

dummy war head of a torpedo to record the behaviour of the torpedo on trial runs.

The galvanometer unit consists - as can be seen in Fig. (33) of a Ticonal magnet, between the pole pieces of which are fixed twelve spring loaded bifilar suspended mirror galvanometers. (Fig.33). Each galvanometer has a single separate terminal, but the second terminal in each case is returned through the magnet and therefore they are all common and cannot be insulated from each other. In using the unit the common return for the galvanometer presented a considerable problem, for the separate pieces of apparatus which were to be connected each had a different standing potential at the output. Nevertheless, to use the galvanometer it was essential that all their inputs should vary about a common potential - preferably earth. This object was achieved by designing a galvanometer input unit (Fig.34), which consisted of four triode bridge circuits. The figure shows one such bridge circuit (V_1) and the built in valve voltmeter V_2 and V_3. The circuit is so arranged that with the input switch in the"balance galvo"position ~~xxxxxxxx~~ (See fig.34), the bridge valve can be balanced so that no voltage is passed across the galvanometer as measured by the valve voltmeter. When the switch is put across to the "input" position, the standing input potential is backed off by applying an equal and opposite potential, whereupon the valve voltmeter again records no voltage drop across the

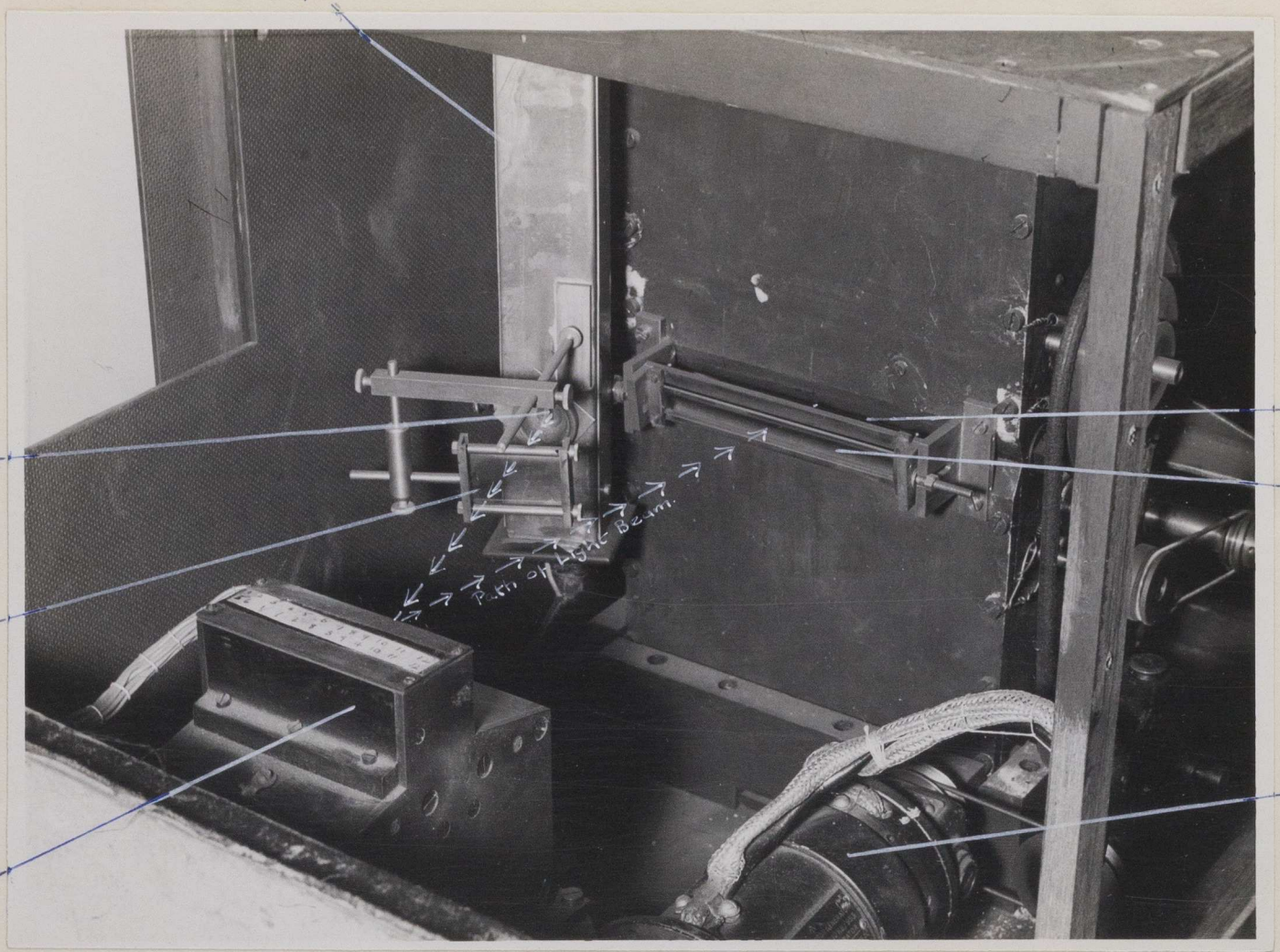


fig 35

Interior of Photographic Recording Unit

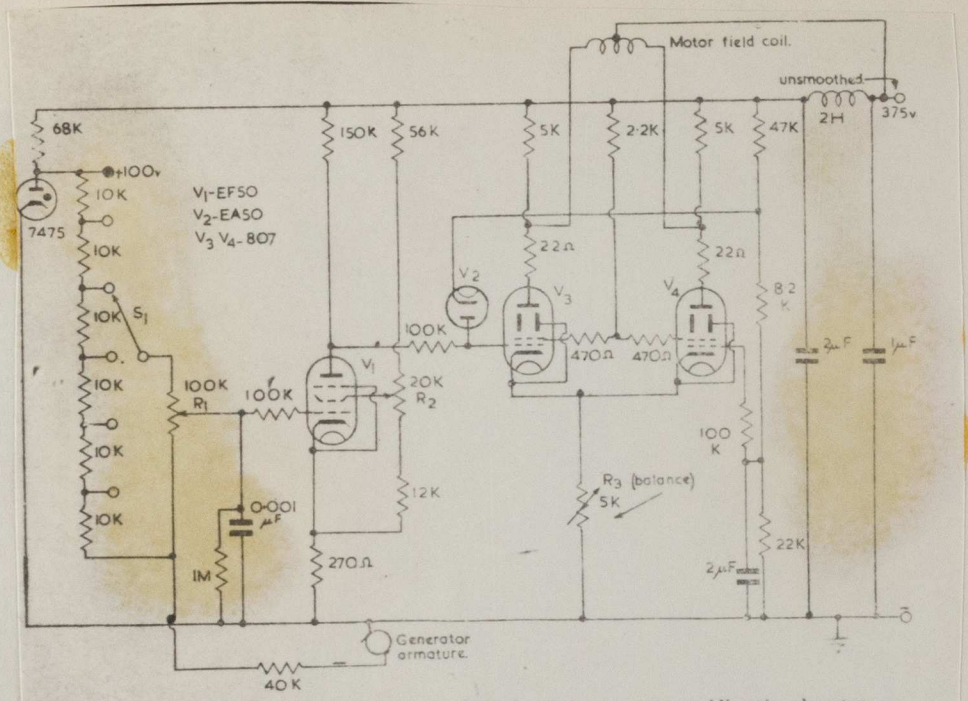


Fig. 51.—Basic velodyne supply and control circuit for use as a unidirectional motor.

fig 36

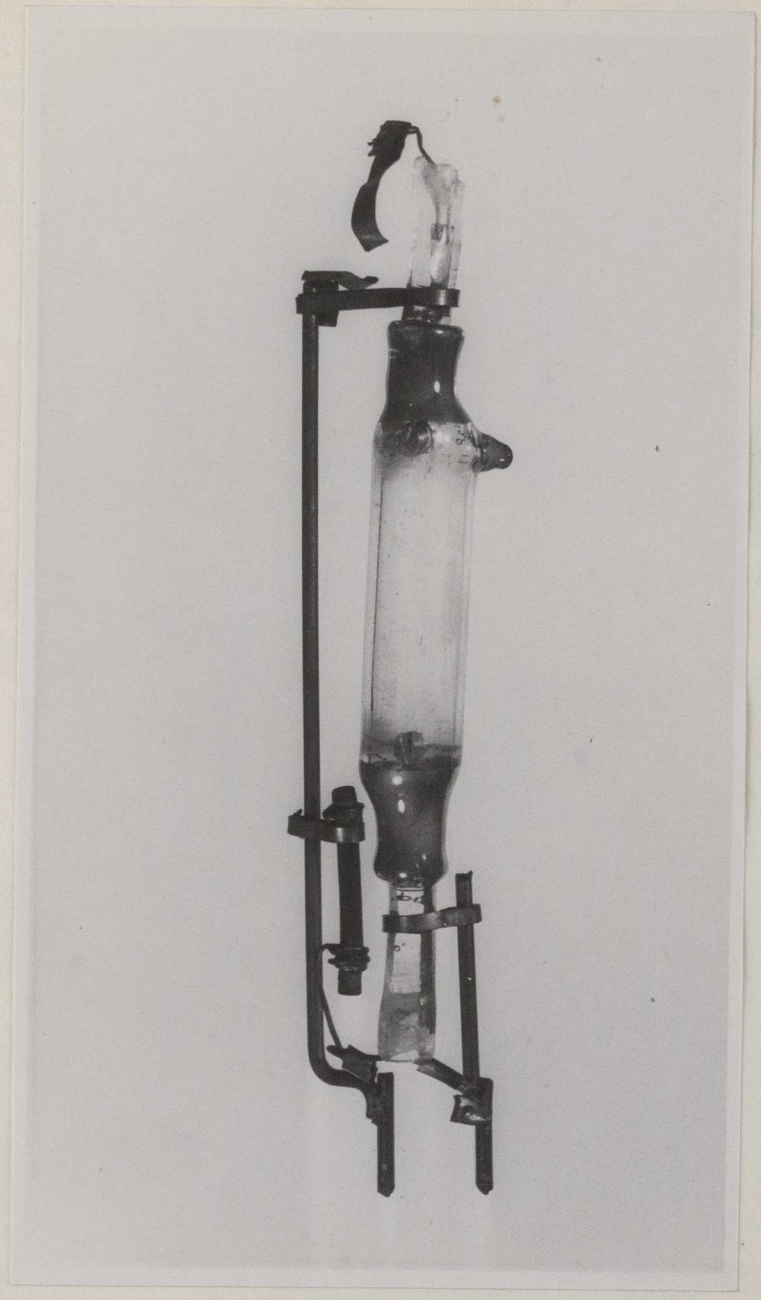


fig 37
Mercury Vapour Lamp (x approx 2)

galvanometer. Now the galvanometer is in the central zero position, and will record variations at the input about the zero input potential.

Unfortunately an Admiralty camera unit was not available so a much more cumbersome but equally efficient light source and camera was made from equipment at hand in the laboratory. The camera (Fig.35) takes 5" wide paper and has a slit five thousandths of an inch wide, the paper is driven through reduction gears from a velodyne motor type 74 which is driven from a control unit (Fig 36 from Dickenson, 1950), to give a wide range of paper speeds. The principle of this motor is that it is a motor and a dynamo on a common shaft, the faster the motor turns the bigger the output from the dynamo. As used at present the output of the dynamo part feeds back to the valves which supply the motor fields and thereby maintains a high constancy of speed. In addition the speed of the motor can be altered between 10 and 2,000 R.P.M. by the turn of a switch on the control unit without any change in the torque of the motor. This motor is the most flexible motor unit we know.

The optical system was as follows. The light source was the capsule out of an 80 watt Ediswan type mercury vapour lamp (Fig.37). Only Ediswan or B.T.H. lamps are suitable for this purpose - other makes were found to be of flimsy construction. These capsules provide a very intense light source of small dimensions and high actinic output. The capsule was mounted in a lamp house with an adjustable slit about 3mm.

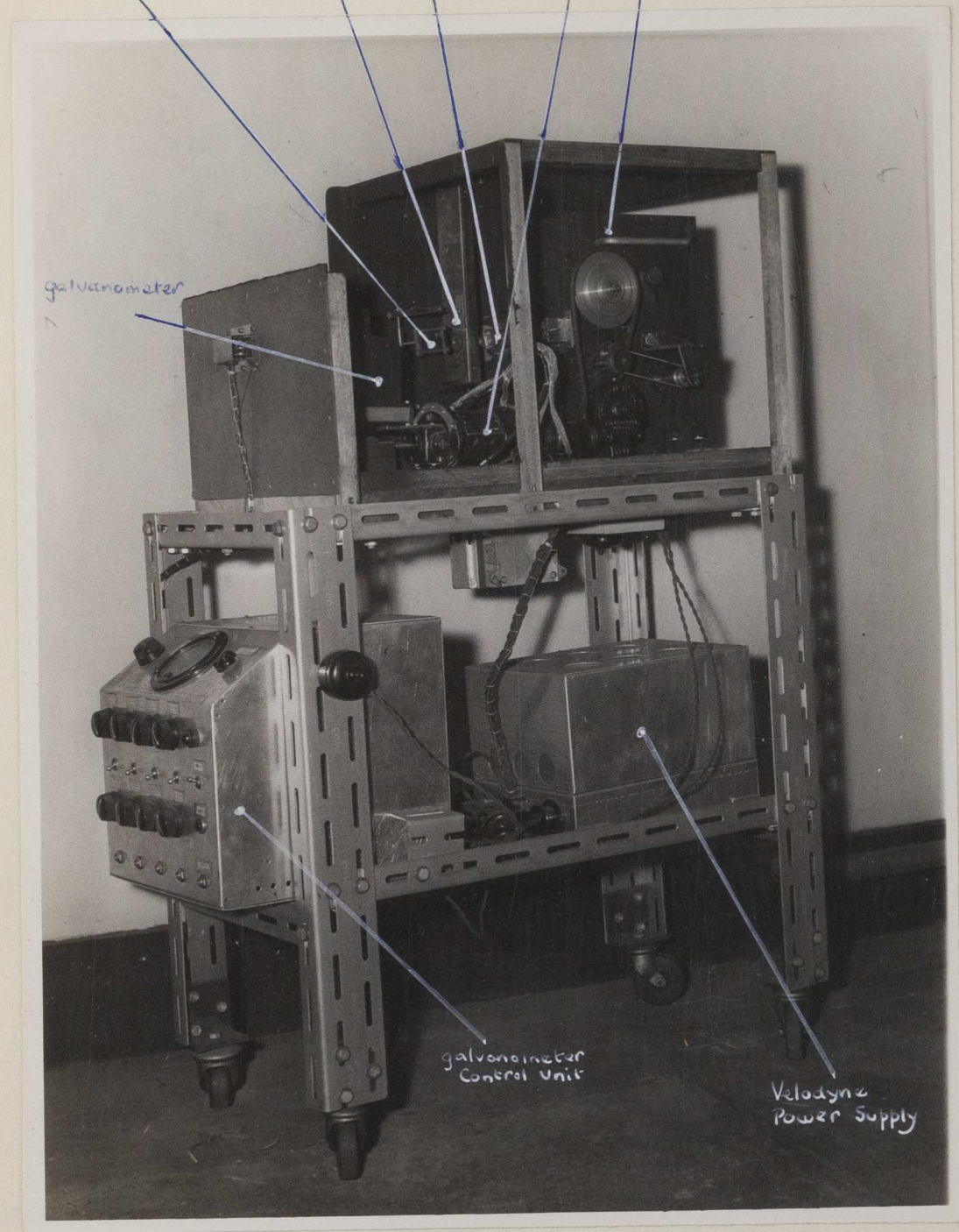


fig 38

Photographic Recording Unit.

away from it. The image of the slit was focussed on to the galvanometer mirrors by a plane-convex cylinder of focal length 1.7 inches with its axis at right angles to that of the slit. The galvanometer mirrors are concave cylinders of 10.9 inches focal length, the axes are parallel with the slit axis and focus an image of the vertical lamp-slit on the camera slit. The intensity of the images falling on the camera slit is further increased by a plane-convex cylindrical lens placed in front of the camera slit with its axis parallel to the slit, and so focussing the images on the camera slit in such a way as to make them shorter in length. This complex description is further elucidated in Fig.(35).

The galvanometer, camera and optical system are all rigidly mounted in a light-tight box. The box is mounted on a "Dexion" trolley together with the motor control unit and the galvanometer input unit. (Fig.38).

PART II

THE COMMON CAROTID ARTERY

FLOW RECORDINGS FROM THE NORMAL CAROTID ARTERY

(i) INTRODUCTION

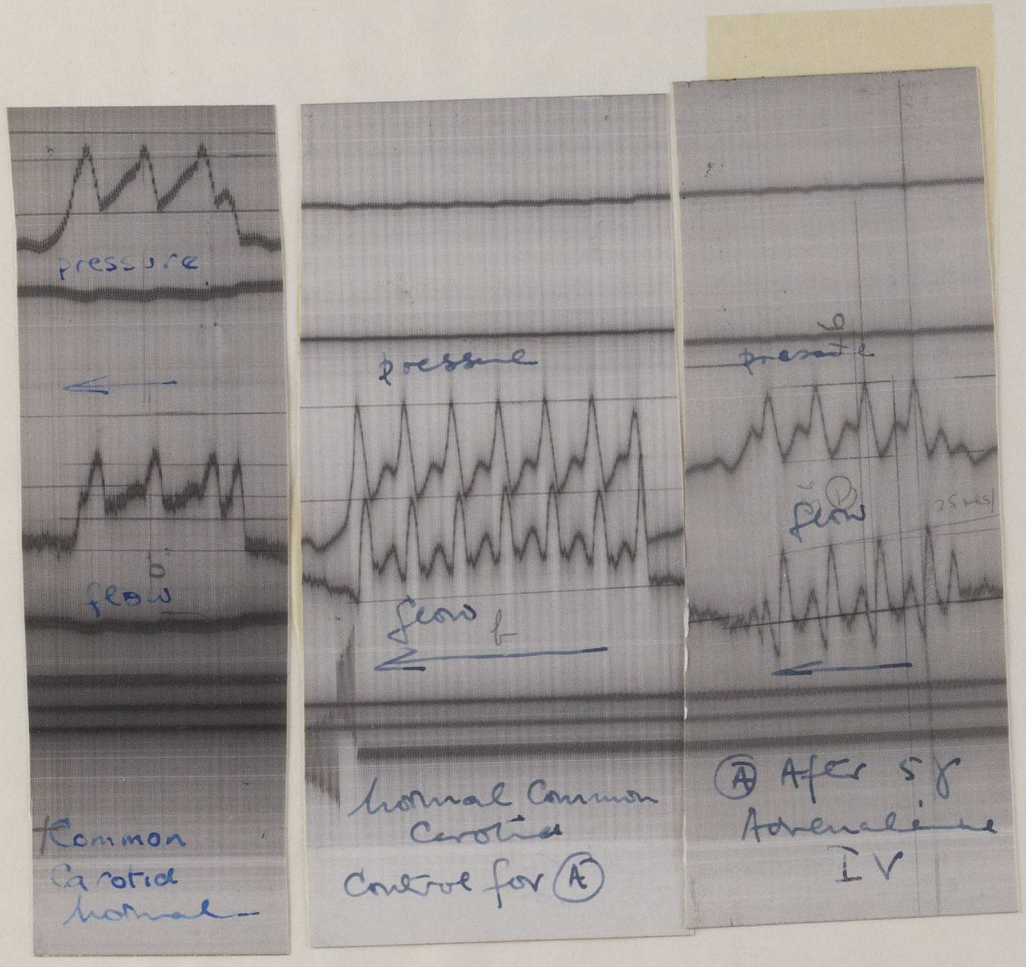
Several authors have published tracings of the blood velocity pulse wave in the carotid artery; Machella (1936) using the hot wire method, Kolin & Katz (1937) using the electromagnetic flow meter, Bergman, (1937) using the stromborste and Shipley et al (1943) using the orifice meter. All the work has been performed on the dog except that of Bergman who used the rabbit. On inspection the records presented by these authors were widely different both in form and in the absolute flow velocities presented. The greatest variations of form were the presence or absence of negative flow or backflow in the traces. Bergman, and Shipley et al (1943) demonstrated backflow but as Bergman used the rabbit his findings are not truly relevant to the discussion of the present work. Some possible faults have already been described in results obtained with the stromborste (p.4.) The other authors do not describe the presence of backflow. It is concerning the question of the presence or absence of backflow that most discussion exists. Shipley et al (1943) laid it down as a principle that, unless the blood velocity pulse ~~backflow~~ record shows backflow the result is of questionable validity. They arrived at the conclusion that backflow is present from results obtained with the orifice meter. They presented two

traces from the carotid artery of the dog. One showed the presence of backflow, the other did not. In addition to these traces they reproduced tracings from other arteries, not all of which showed backflow. They also considered that the results obtained by Green (1940) from the coronary arteries (which showed backflow) corroborated their own results. However, results obtained from coronary arteries, which are exposed to very rapid changes in peripheral resistance due to the contraction of the heart, may not properly be compared with the blood flow in the other peripheral arteries. Further, as will be seen in Fig.(10) the experimental arrangement used by Green et al ~~in~~ requires so much interference with the normal vascular supplies that on these grounds, comparison with other work is difficult.

The method used by Machella (1936) is not capable of demonstrating reversal of flow in an artery, hence his results could be spurious. The results of Kolin & Katz (1937) using the electromagnetic flow meter which is capable of demonstrating backflow have to be considered more seriously. Shipley et al (1943) considered that this method of recording blood flow was inaccurate for two reasons:- (1) that the frequency response of the instrument is inadequate and (2) that the constricting cuff damps out the high frequency flow changes in the artery. (1) The apparatus used by Kolin and Katz(1937) may have had too low a frequency response for they used the A.C. electromagnetic flow meter, from which the results are represented as a modulated 60 cycles/sec. wave. On the other

hand, if the duration of the negative flow wave in the record Shipley et al, published is measured and if it be assumed that it is 180° of a sine wave, the frequency of this wave is approx. 20 cycles/sec.; therefore, the electrical part of Kolin's apparatus should be able to record this wave. To overcome all possible doubts on this point the D.C. electromagnetic flow meter should be used. (2) The contention that the cuff of the electromagnetic flow meter can cause the high frequency changes in the blood flow to be damped out, deserves consideration. It must be pointed out that the orifice meter acts as a cuff in that it makes a part of the artery rigid and also constricts the artery to a greater degree than does a properly fitted arterial cuff of the electromagnetic flow meter.

The tracings given in this thesis have been prepared by projecting the actual experimental tracings with an epidiascope on to photographic paper. The relevant parts of the tracings were then drawn over with waterproof indian ink and the photographic image then bleached out. The figures shown below are parts of actual experimental tracings and show the type of record obtained.



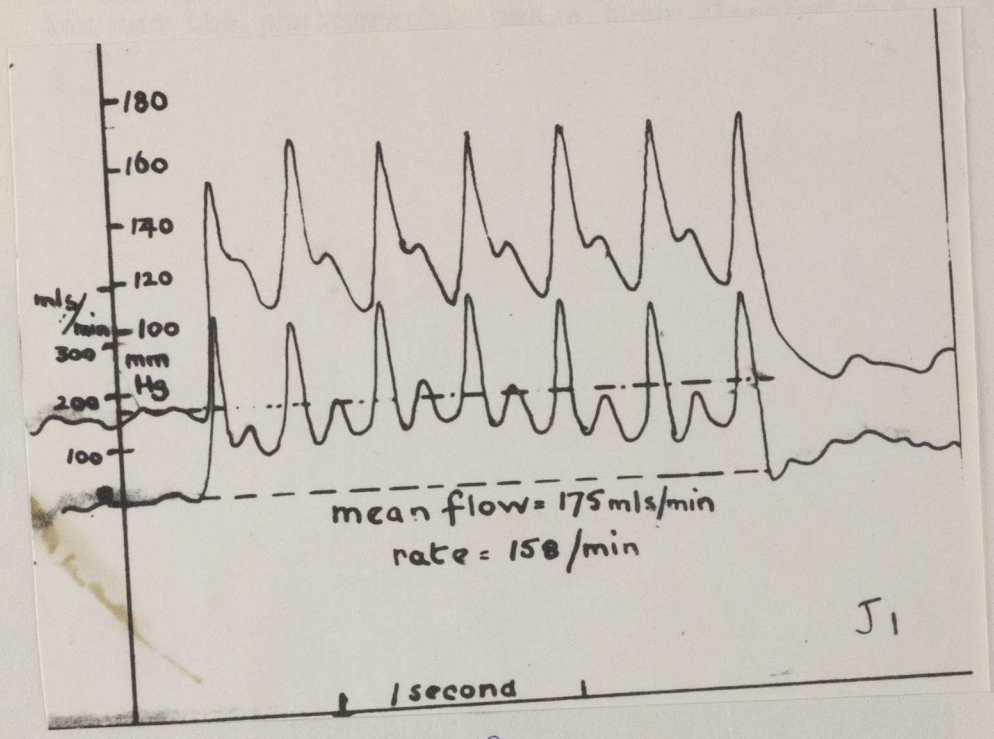

180
160
140
120
100
mls/min
300
mm Hg
200
100
mean flow = 175 mls/min
rate = 15 8/min
J1
1 second

fig 39 a.

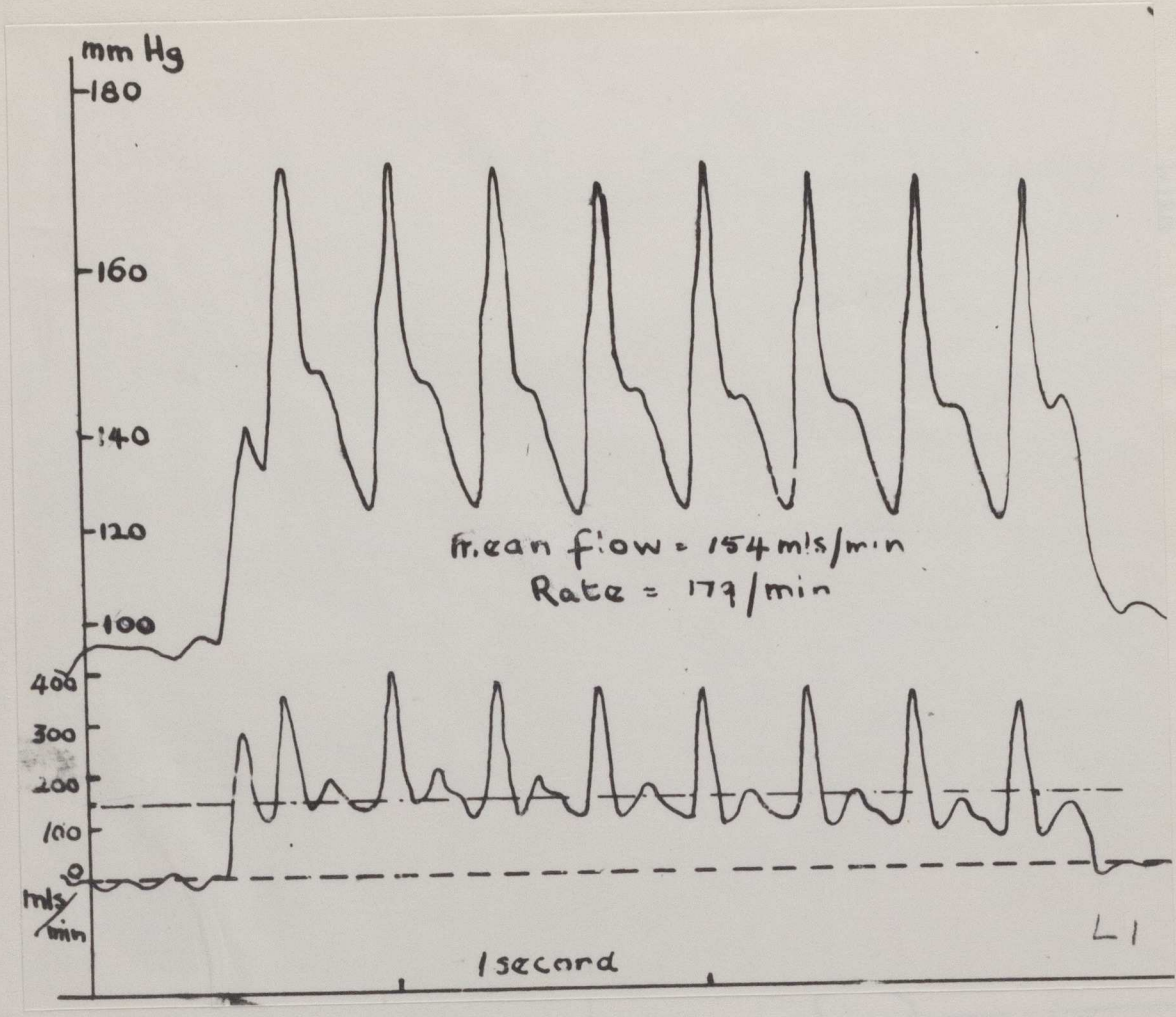

mm Hg
180
160
140
120
100
400
300
200
100
0
mls/min
Mean flow = 154 mls/min
Rate = 179/min
1 second
L1

fig 39.

(I) MAX. & MIN. flow VELOCITIES FOR NORMAL CAROTID .

	Wt.	Max. ml/min	Min. ml/min	Mean ml/min
G.	12.4 Kg.	126	52.5	65.7
H.	8.0 Kg.	74	27	60.0
I.	11.5 Kg.	187	52	92.5
J.	11.2 Kg	325	100	175.5
K.	27.0 Kg.	173	46	94.3
L.	12.5 Kg.	405	111	154.0
M.	9.0 Kg.	395	190	-
N.	13.2 Kg.	236	123	
O.	9.2 Kg.	216	54	92.1

EXPERIMENTAL RESULTS

The Carotid Velocity Pulse Wave (Fig.39).

The most striking characteristics of the velocity pulse wave of the carotid artery is that all the variations in velocity are well above the base line and that at no time during the pulse cycle does flow cease or reverse its direction. The wave consists of two main portions, the systolic part and the diastolic part. The systolic rise in the velocity pulse begins about .02 secs. before the systolic rise in the pressure pulse and achieved its maximum whilst the pressure pulse is still rising. It then falls to its minimum. The dicrotic portion of the velocity pulse wave consists of two or three oscillations but the tendency is always downwards. These oscillations do not appear to correspond to any variations in the pressure in the artery.

The form of the velocity pulse recorded is fairly constant but the flow velocity of the blood travelling along the artery varies from dog to dog. No correlation between the ~~velocity~~ flow and the weight of the dog could be made, the biggest dog used weighed 27 Kg. and had a maximum ~~velocity~~ flow of 173mls/min., a minimum ~~velocity~~ flow of 46mls./min. and a mean ~~velocity~~ flow of 94.3mls/min., whereas the greatest ~~velocities~~ flows recorded were in a dog weighing 12.5 Kg. which had a maximum ~~velocity~~ flow of 405mls./min., a minimum of 111mls./min. and a mean of 154 mls./min. Table I gives some of the results obtained.

These results are in agreement with those obtained by

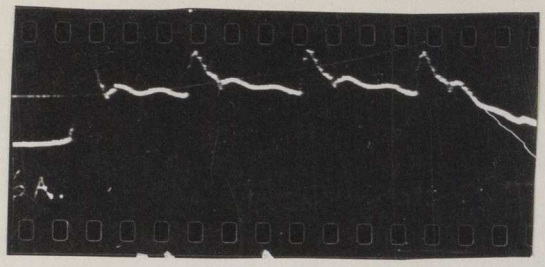


fig 40
Control

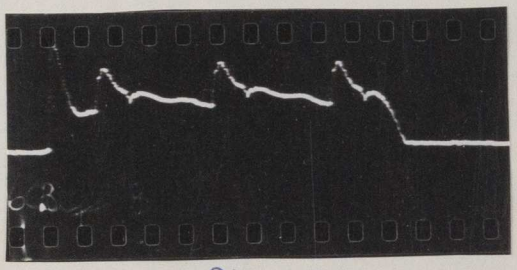


fig 41
with extra cuff distal

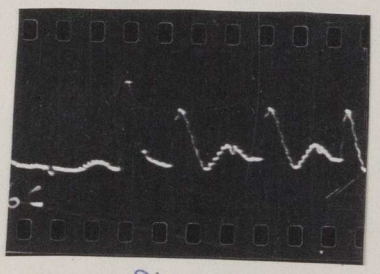


fig 42
with ligature loosely applied

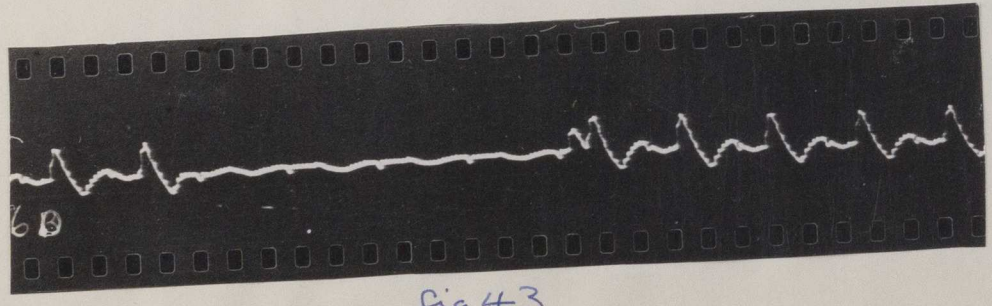


fig 43
as fig 42 but with tighter ligature

Kolin & Katz (1937) and in striking disagreement with those of Shipley et al (1943). As these latter workers have criticized the electromagnetic flow meter, their criticisms must be met before validity of the results here described can be accepted. The frequency response of the flow meter has already been described and has been shown to be adequate (p.27), but the effect of the cuff on the velocity pulse wave has yet to be investigated.

If the arterial cuff surrounding the artery has a serious effect on the blood flow in the artery, the placing of a second slightly smaller cuff above or below the recording cuff should have an effect on the velocity trace recorded. Fig (40) shows the results obtained when using a cuff 3.5mm. in diameter as the recording cuff. Fig. (41) shows the effect of placing a cuff 3.25mm. diameter distal to the recording cuff. It will be seen that this manoeuvre has no appreciable effect on the velocity trace recorded. The pressure recorded when the two cuffs were in place did not differ from that recorded when one cuff was in place (the manometer was distal to both cuffs).

From these results it would seem that the absence of backflow from the recorded traces was not due to the flow meter used. (The instrument can record backflow in a velocity trace as will be seen in the results obtained after the administration of adrenaline). However, the experiments do not ~~xixx~~ explain why the orifice meter records backflow in the normal carotid artery. Recordings after the administration of Adrenaline always show backflow, and this indicated a possible

II

COMMON CAROTID FLOW

Dog + wt.	flow ml/min	Mean ml/min.
A. 14.3 Kg.	259.4	206
	154.0	
B 7.5 Kg.	84	84
	84	
C. 9.3 Kg.	80.7	70
	82.0	
	59.7	
	63.0	
	73.4	
	59.0	
D 12.5 Kg.	91.0	59.5
	81.5	
	46.8	
	41.7	
	38.9	
	51.5	
	65.1	
G 12.4	65.7	85
	83.3	
	71.6	
	76.3	
	89.3	
	122.8	
H 8 Kg.	59.6	61
	62.5	

Dog + Wt.	flow ml./min.	
I 11.5 Kg.	92.5	
	86.5	101 mls/m
	124.1	
J 11.2 Kg.	155.0	
	120.2	116.5 "
	175.3	
K 27.0 Kg.	94.3	
	67.6	122 "
	81.9	
	118.8	
	125.2	
L 12.5 Kg.	154	
	102	125 "
	119	
N 13.2 Kg.	120.8	
	147.8	134 "
M 9 Kg.	181	
	216	
	251	189 "
	218	
	206	
	152	
	165	
	121	

cause of the backflow recorded by Shipley et al. Adrenaline acts as a vasoconstrictor, so possibly the constriction made by the orifice meter caused backflow. This hypothesis was tested by partially ligating the carotid artery whilst recording velocity with the electromagnetic flowmeter; as the degree of ligation increased the form of the velocity pulse wave changed and the wave form became much more oscillatory (fig. 42) until a wave of backflow was present. (Fig.43). Thus by partially constricting the artery a backflow component was made to appear in the velocity pulse wave. A replica of the orifice meter used by Shipley et al (1943) was made and tied into the carotid artery above the recording cuff. When the screw was tightened it was found that this had the same effect as ligating the artery. It is therefore concluded that in the presence of severe arterial constriction as is found in the orifice meter, the recorded velocity pulse is likely to contain artefacts due to the recording instrument. From these experiments it will also be seen that differing degrees of constriction give different forms to the velocity wave and if the experimenter considers that backflow is always present in the velocity pulse wave he has only to alter the size of the orifice until backflow appears, although he may consider this procedure to be that of obtaining "the desired sensitivity". Table II contains details of volume flow recorded along the carotid artery in these experiments. The results obtained by other workers show a smaller flow than is here described; the reason for this is not fully apparent - we have criticised

fig 45

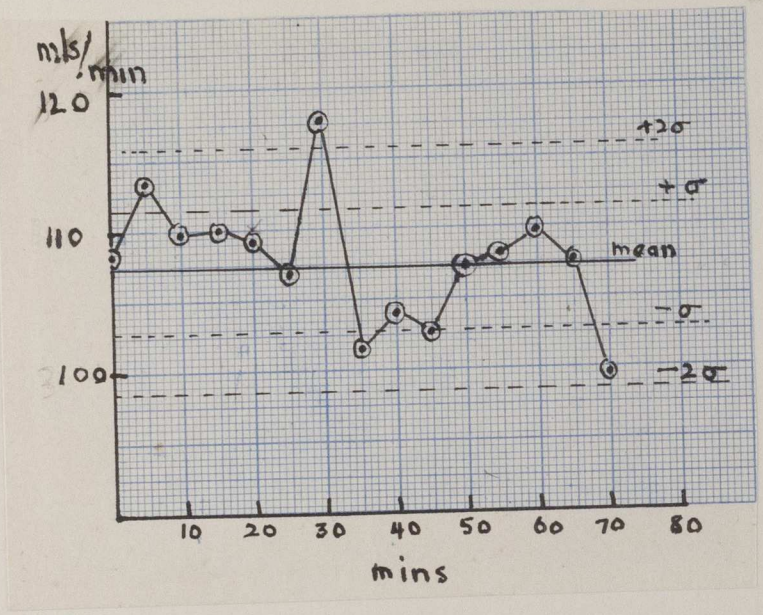
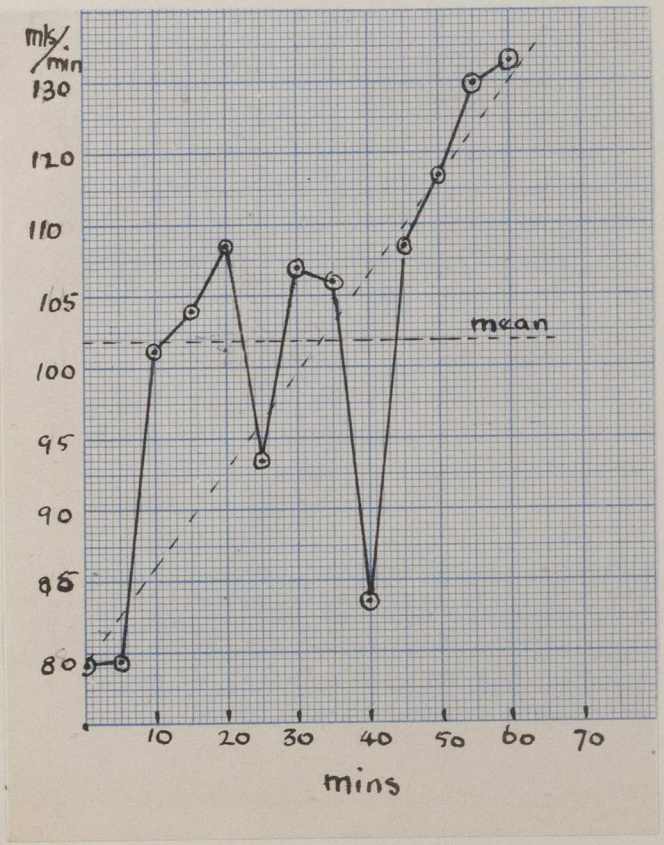

mls/min
120
110
100
+2σ
+σ
mean
-σ
-2σ
10
20
30
40
50
60
70
80
mins

fig 44


mls/min
130
120
110
105
100
95
90
85
80
mean
10
20
30
40
50
60
70
mins

the orifice meter sufficiently already, but again it is believed to be at fault in that it cuts down the total flow of blood through itself.

The Variation in Blood Flow in a single dog.

In the earliest experiments performed it was discovered that the blood flow in the common carotid varied a great deal without any external stimulus being applied to the dog, or without any change in the mean blood pressure (the condenser manometer unit had not been made and a mercury manometer was used). This was not altogether unexpected, for the blood pressure level in an animal is the resultant of the total peripheral resistance of the dog and the cardiac output, and if one part of the peripheral resistance increases, another could reciprocally decrease and thereby maintain a constant blood pressure. In addition, as the dog is anaesthetized the level of anaesthesia will be constantly varying as the animal metabolizes the anaesthetic agent. Experiments were performed to study the long term changes in blood pressure and flow in the dog. Typical results are shown in Figs. (44,45). Records were taken every 5 mins. for over an hour. The curves represent the two types of results obtained. The first shows a fairly constant blood flow with a constant B.P. and the second shows a steady increase in flow with a steady B.P. The results were statistically analysed. In Fig.44 all the results except one lie within twice the standard deviation of the mean. This would signify that variations was of no significance. Further,

the χ^2 test was applied to the results to test whether the amount by which each of the blood flow results diverged from the mean chance or was significant. It was found that variations from the mean were such that P lies between 0.8 and 0.9 and therefore it can be assumed that the variations were chance. In the case of the second curve, fig.45, five out of twelve observations fell outside twice the standard deviation of the mean - therefore some significant change was taking place. A sloping straight line was drawn which fitted the points and the variation of the observations from this line was tested by the χ^2 test and it was found that P = 0.3 - 0.5, and therefore it could be said that the variations from this line could be random. The cause of this steady increase in blood flow could not be elucidated but whatever it was it showed that considerable changes could take place in the blood flow in an apparently normal animal.

In the light of these experiments it was decided that any blood flow measurements obtained from an experimental procedure should only be compared with a control made immediately before the experiment was made. Therefore all the results given are accompanied by controls obtained usually about 1 minute before the experiment begins. Even so (as will be described later), small changes in blood flow take place from heart beat to heart beat. The blood flow results given are usually the means of about three to six consecutive heart beats, never less, sometimes more.

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VELOCITY CHANGES IN THE CAROTID AND FEMORAL ARTERIES OF DOGS DURING THE CARDIAC CYCLE

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(*Received* 9 *November* 1951)

A difference of opinion exists concerning the form of the phasic flow pattern in peripheral arteries. In particular there is some uncertainty as regards the importance and frequency of occurrence of 'negative' (i.e. back) flow in certain of these vessels. In the experiments to be described, phasic flow has been recorded by an electromagnetic method, not only in order to examine the phasic flow in unopened vessels recorded by this method, but also to test some of the possible errors which it has been suggested may be involved (Shipley, Gregg & Schroeder, 1943).

METHOD

The principle of electromagnetic induction was first applied to the measurement of instantaneous blood flow by Wetterer (1938) and independently by Katz & Kolin (1938). The electromagnetic induction of an e.m.f. depends upon the fact that when a conductor of length l cm moves with a velocity of v cm/sec through a magnetic field of H gauss, an e.m.f. of e volts is induced, such that

$$e = Hvl\ 10^{-8}. \qquad (1)$$

Wetterer (1937) and Katz & Kolin (1938) have shown that the blood in an artery may be considered as the moving conductor in these circumstances, and that the induced e.m.f. is conducted to the outer surface of the artery.

In such a case the internal diameter of the blood vessel is equivalent to the length of the conductor. In order to measure the velocity of the blood, the diameter of the artery and the field strength of the magnet must remain constant. This is achieved by placing a Perspex cuff around the artery, so that it retains its diastolic diameter, and by using a permanent magnet of high flux density. The induced e.m.f. is then directly proportional to the velocity of blood flow within the vessel (eqn. 1). In these conditions the diameter of the blood vessel remains constant, so that the volume flowing in unit time is proportional to the velocity and, provided the response curve of the instrument is linear, is proportional also to the area enclosed between the recorded velocity curve and the base-line.

Apparatus

The essential parts of the electromagnetic flowmeter consist of an arterial cuff, a magnet, non-polarizable electrodes, and a suitable electrical recording system.

The arterial cuff (Fig. 1*b*) is made of Perspex, and is in two parts. When assembled it encloses the artery, and fixes the position of the magnet in such a way that the magnetic field, the direction of blood flow, and the axis across which the potential difference is measured, are at right angles to each other.

To accommodate arteries of different sizes a set of cuffs was made with arterial channels of graduated size, each differing by 0·25 mm in diameter. The permanent magnet used is shown in Fig. 1*c* and was made of Alcomax III (Messrs Jessop, Sheffield) with mild steel pole-pieces having a 5 mm gap. The field across the gap was 1950 G. In use the magnet is covered by a thin rubber finger stall and thus insulated.

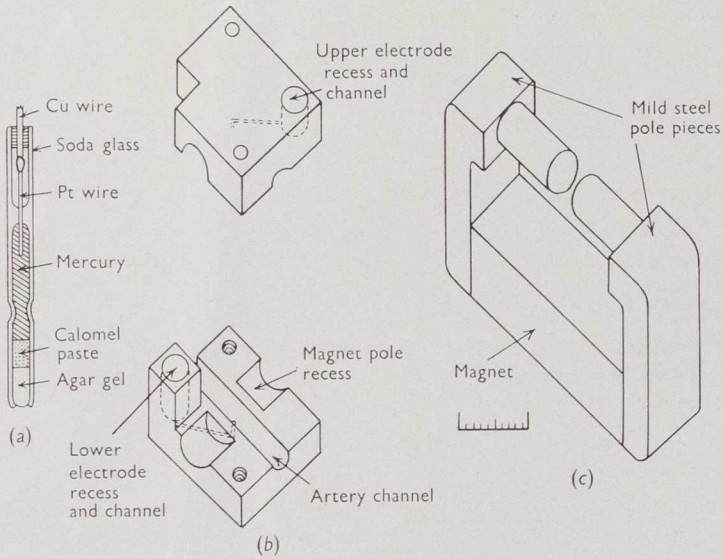

Fig. 1. (*a*) non-polarizable calomel electrode; (*b*) upper and lower halves of artery cuff; (*c*) magnet; scale: 10 mm.

Calomel half-cells have been found to be the most satisfactory electrodes. They were constructed so as to minimize the overall size (Fig. 1*a*). In use the electrodes were inserted into retaining holes in the Perspex cuff, and contact with the vessel wall was made in the correct plane by holes drilled in the cuff and filled with agar-saline gel (2% agar in 0·9% (w/v) NaCl).

This construction ensured that mechanical displacement of the components relative to each other did not take place, and that drying of the gel and artery wall was minimal. The electrodes were connected to a conventional push-pull direct-coupled amplifier, having a maximum voltage gain of $1{\cdot}5 \times 10^6$, and a frequency response which was linear up to 1000 c/s. The amplified e.m.f. was displayed on a cathode-ray oscilloscope, and records were made using a moving film camera. The frequency response of the amplifier was linear up to 1 kc/s, and Fig. 2 shows that the amplifier-electrode system responded to rapid changes in velocity. When measured, the uprising slope of these waves corresponded to a frequency of 180 c/s.

Whether damping was introduced by the recording unit or not was determined by the application of a second cuff 0·25 mm smaller in diameter, either above or below that from which recordings were made. Fig. 3 shows records taken with and without a second cuff. There is no significant difference between volume, or wave-form, in either case.

RESULTS

Calibration

The interpretation of the recorded velocity trace depends upon the satisfactory calibration of the instrument. In the conditions of the experiments the calibration curves should be linear, and should pass through the origin; known

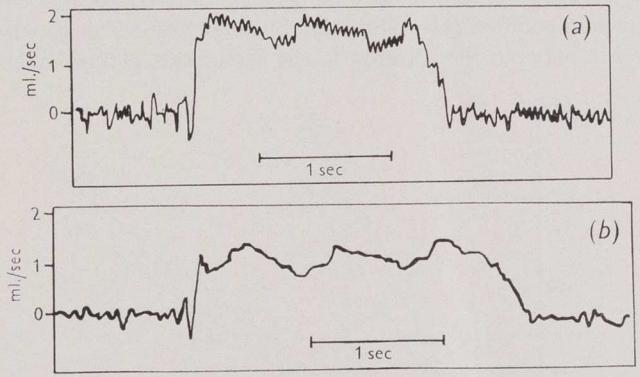

Fig. 2. (*a*), (*b*) saline inflow intra-arterially injected. The volume in each case is the same but perfusion pressure is different, consequently velocity of inflow differs in each instance. Figs. 2, 3, 6, 7 and 8 are tracings of photographic records.

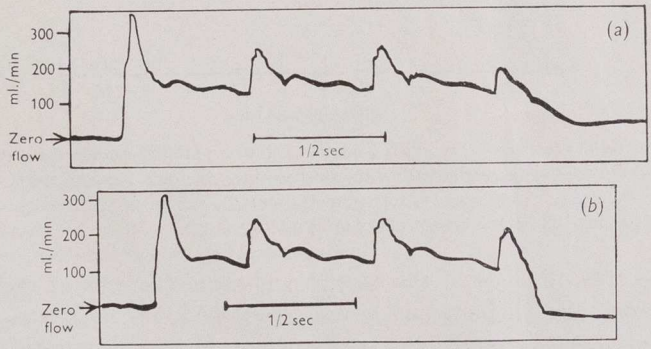

Fig. 3. (*a*) normal trace of carotid flow; (*b*) trace from same, the artery as in (*a*) but with addition of cuff 0·25 mm smaller than recording cuff.

volumes injected through the unit should give good agreement with recorded areas, which should be independent of the velocity of inflow. The e.m.f. induced by equal velocities, either forward or backward, should be equal in quantity but of opposite polarity.

The above considerations were examined separately in relation to the carotid and femoral arteries of dogs. Ten dogs were used, with weights between 9 and

15 kg, anaesthetized with sodium pentobarbitone (32 mg/kg) administered intravenously. A suitable cuff was applied to the artery, and blood velocities were recorded at a convenient amplification, which was then kept constant throughout the experiment. The artery was cannulated as near as possible to the distal end of the cuff, a burette was connected to the cannula, and both were filled with 0·9% saline. Air pressure was applied to the upper surface of the saline in the burette, and on opening the burette tap measurable volumes of saline flowed into the vessel, at a velocity which depended upon the difference between the pressure in the artery and burette. Fig. 2 shows

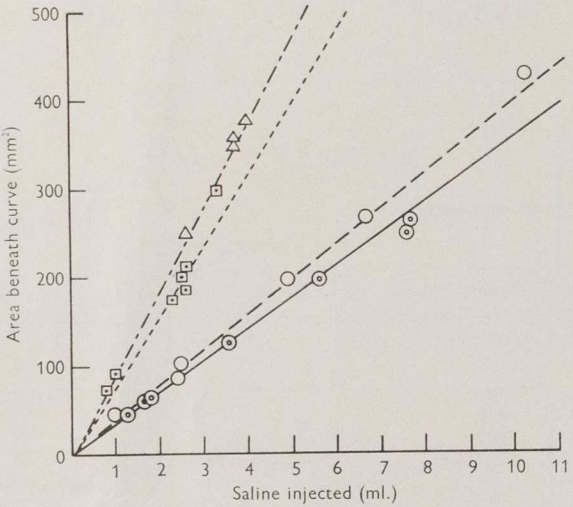

Fig. 4. Four calibration graphs in which volumes of flow are plotted against the area enclosed between the velocity traces due to flow and the base line. △, dog 8, femoral artery, retrograde saline; ○, dog 8, carotid artery, retrograde saline; ⊙, dog 6, carotid artery, retrograde saline; ⊡, dog 10, femoral artery, efflux of blood.

typical records obtained in this way. To measure the area of the curves, tracings from the photographic records were made on millimetre-squared paper. Retrograde flow of saline was chosen for calibration because it prevents the collapse of the vessel between recordings, and the subsequent inevitable violent distension which would have introduced an artifact due to potentials caused by movement. It will be seen that the curve recorded is not flat-topped, but shows velocity variations due to the intravascular pressure changes during the pulse cycle, as a consequence of which the difference in pressure between the burette and the vessel varied.

This procedure was carried out on seven dogs and typical results obtained are shown graphically in Fig. 4. It may be seen from these results that the

correspondence of area to injected volume is good, and that the curves pass through the origin.

During the pulse cycle the velocity of blood flow varies considerably; hence it is important to consider whether variations in velocity affect the calibration of the instrument. Using the experimental arrangement described above, saline was injected into the artery at a number of different pressures, thus altering the inflow velocities. Fig. 2 shows a recording made when the same volume of saline was infused at two different velocities. It was found that the areas/ml. enclosed by the curves were identical.

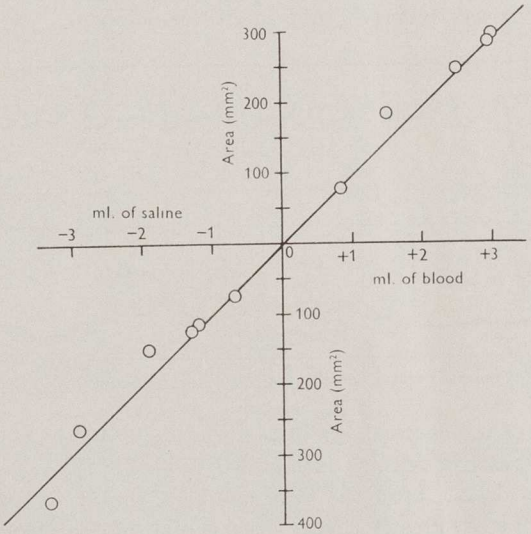

Fig. 5. A calibration curve in which the efflux of measured volumes of blood is plotted against the area enclosed by the corresponding velocity trace and the base-line, and a retrograde saline calibration immediately following this in the same animal. The signs + and − indicate reversal of flow in the two parts of the graph.

There remained two possible sources of error in calibration; that a calibration made with saline would not be applicable to blood, and that the direction of calibrated inflow was retrograde. To estimate the significance of both these factors, experiments were performed in which measured amounts of blood were allowed to escape through a needle-valve which was tied into the artery distal to the cuff. The rate at which blood escaped did not alter the intra-arterial pressure. Immediately following this procedure saline solution was perfused through the needle valve, and a retrograde calibration made in the usual manner. Fig. 5 shows the results of such an experiment. Both groups of points lie on a straight line passing through the origin, but with a reversal

of polarity as a consequence of flow reversal. In saline calibration, velocities of saline flow were used which covered the range of velocities found in the intact artery. It was concluded that the method was valid for measurement of blood flow at the velocities and pressures encountered physiologically, whether flow be towards the periphery or not.

Carotid artery: normal flow

Fig. 6 shows typical blood velocity curves for the intact carotid and femoral arteries in a dog. A level for zero flow was recorded during a brief closure of the vessel by means of a narrow clip, immediately distal to the cuff. A continuous base-line was drawn through successive points.

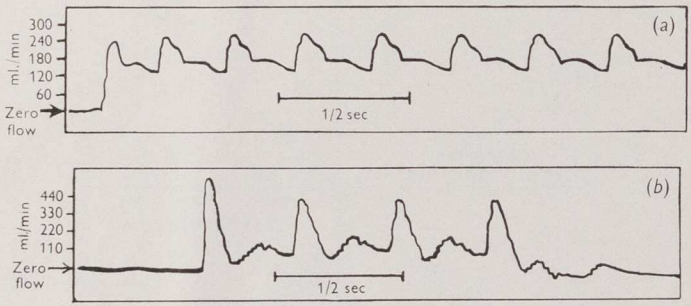

Fig. 6. (*a*) normal carotid velocity trace; (*b*) normal femoral velocity trace.

The pattern of the curve shows little variation in different dogs. There is a very rapid increase in velocity during the first part of the velocity cycle and a more gradual decline after the peak has been passed. At the maximum velocity there was frequently a very brief period during which the velocity remained almost constant, subsequently falling rapidly to a plateau showing small variations in velocity; but, in general, the velocity decreased over this diastolic period until the next systole commenced. In none of the traces in this series of experiments was there any indication of 'negative' velocity, i.e. back-flow.

Table 1 shows seven values of the maximum, minimum and mean carotid flows in four dogs. These values were determined by reference to calibration curves using retrograde inflow of saline, as has already been described.

Femoral artery: normal flow

A typical record of femoral arterial blood velocity curve as shown in Fig. 6*b* differs from the carotid artery curve, in that the drop in velocity from the systolic peak is steeper, and is continued until a velocity is reached which is equal to, or less than, the velocity at the beginning of systole. Following this there are velocity variations of comparatively small size until the commence-

ment of the next systolic increase in velocity. No back-flow was observed in any of these experiments on the femoral artery. Table 1 shows the minute volume of flow in the femoral artery determined by the above method of calibration.

TABLE 1.

Expt. no.	Dog	Artery	Peak flow (ml./min)	Minimum flow (ml./min)	Pulse volume (ml.)	Mean flow (ml./min)	Heart rate (beats/min)	Experimental conditions
1	4	Carotid	382	200	1·5	270	180	Normal
2		Carotid	362	190	1·6	262	164	Normal
3		Carotid	190	−52	0·2	52	258	Adrenaline, 180 μg
4		Carotid	227	−87	0·22	51	230	Adrenaline, 180 μg
5		Carotid	230	36	0·35	79	225	Acetylcholine, 20 μg
6	6	Carotid	200	100	1·3	140	108	Normal
7		Carotid	200	100	1·3	140	108	Normal
8		Carotid	192	90	1·2	131	109	Normal
9	8	Carotid	404	98	1·15	214	186	Normal
10		Carotid	515	−74	0·5	82	164	Adrenaline, 100 μg
11	9	Carotid	111	41	0·5	66	133	Normal
12	7	Femoral	452	94	1·5	180	120	Normal
13		Femoral	440	98	1·4	170	120	Normal
14		Femoral	350	−140	0·21	35	140	Adrenaline, 140 μg
15		Femoral	510	75	1·1	140	128	Acetylcholine, 15μg
16	8	Femoral	415	68	1·3	195	150	Normal
17		Femoral	198	−61	0·4	58	144	After moderate constriction with ligature. See Fig. 8*a*
18	8	Femoral	151	−67	0·1	15	144	After severe reconstriction with ligature. See Fig. 8*b*

The effect of drugs

Adrenaline. Fig. 7*a* shows the appearance of the blood velocity wave in the carotid artery after the intravenous administration of adrenaline. The traces differ from the normal pattern since there is a phase in each cycle when back-flow is present. The volume of back-flow depended upon the adrenaline dosage (a maximum of 250 μg was given), but was at all times unequivocal. Peak velocity was equal to, and sometimes greater than, normal (Table 1), but velocity at the end of diastole was usually very nearly zero. The peak 'negative' flow was usually between 100 and 200 ml./min and the mean flow in these circumstances was also reduced (Table 1).

Acetylcholine. Fig. 7*b* shows a trace of carotid artery blood flow after the intravenous administration of 15 μg acetylcholine. This differed again both from the normal traces and those following adrenaline administration. The onset of the systolic wave was clearly divided into two parts, the first having a steeper gradient than the second. The descending portion of the velocity wave was of uniform gradient and was not as steep as the onset wave. The diastolic interval was taken up by a low amplitude positive wave of smooth contour, and there was often a low velocity plateau immediately preceding the onset of the following systolic rise. The peak velocities were 400–500 ml./min.

The diastolic and the mean flows were intermediate in value between the normal and those found after adrenaline administration. Negative flow was not characteristically seen, and when it occurred was small (Table 1).

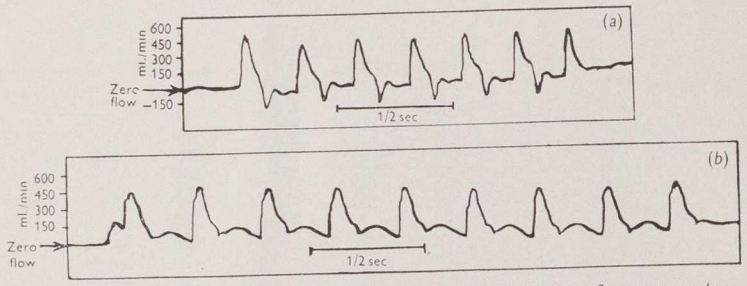

Fig. 7. (*a*) velocity trace from carotid after 200 μg of adrenaline; (*b*) trace from same artery as (*a*) after 20 μg of acetylcholine.

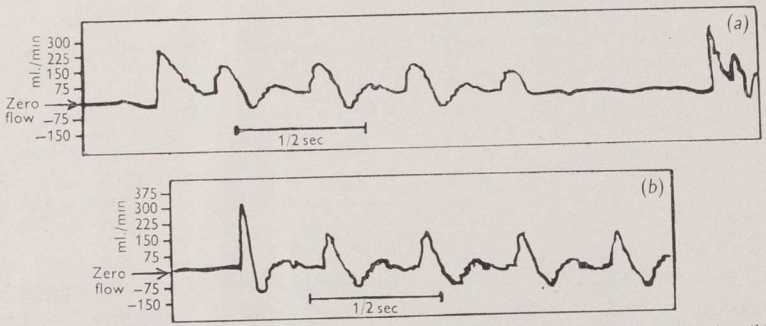

Fig. 8. Dog 8, wt. 13 kg. Velocity patterns in the femoral artery after partial obstruction (blood flow peripheral to the cuff). In this experiment normal femoral flow was 195 ml./min; after 100 μg of adrenaline, 87 ml./min. In (*a*) above, flow is 58 ml./min and in (*b*) 15 ml./min.

Mechanical interference with blood flow

Fig. 8 shows the changes in the record which followed the partial obstruction of blood flow in the femoral artery, by the application of a fine thread ligature distal to the cuff. Mean flow was at once much reduced, and in general the traces resembled those which followed the administration of adrenaline, back-flow being a marked feature of the records.

DISCUSSION

The results here presented for normal carotid and femoral blood flow agree with those obtained by Katz & Kolin (1938) using an electromagnetic flowmeter. Wetterer (1937) has also investigated blood velocity in the ascending aorta of dogs, cats, rabbits and monkeys using a similar method but gives no

data for peripheral arteries. Although the frequency response of their apparatus was limited to below 50 c/s the minute flow volumes published by Katz & Kolin (1938) are in good agreement with the present results (Table 1), and the general outline of their traces is similar.

Shipley *et al.* (1948) measured flow velocities in the carotid and femoral arteries of dogs with an orifice-meter and claimed to demonstrate 'negative' flow in normal circumstances. They suggested that Katz & Kolin had not been able to show the back-flow component because the electromagnetic flowmeter introduced mechanical damping and removed velocity variations of high frequency or lagged in the detection of changes in e.m.f. caused by variation in velocity.

In control experiments we have found no evidence that the calculated velocity was affected by placing a slightly smaller cuff either above, or below, the recording cuff. Only when a much greater constriction was applied, as when the artery was partially ligated, were marked alterations in flow and pattern observed.

It has already been said that the frequency response of the amplifier used is linear up to 1 kc/s and it seemed unlikely that harmonics above this frequency are of importance, the highest frequencies in the pressure wave being 100 c/s (Wiggers, 1928). However, the characteristics of the electrode assembly might have been responsible for a falling off in response at higher frequencies, but no evidence of this was found. For example, in the calibration experiments the retrograde injection of saline produced a change in flow velocity which was approximately in the form of a square wave (Fig. 2).

It seems that the minute volume flows in the carotid artery are higher when recorded by the electromagnetic flowmeter, as in the present experiments and in those of Katz & Kolin (1938), than when the orifice-meter is used (Shipley *et al.* 1943). The difference in flow volume recorded by the electromagnetic flowmeter and the orifice-meter are due to the lower diastolic and systolic velocities and to the back-flow recorded by the latter method, when applied to normal flow. It seems possible that an orifice-meter may introduce a significant resistance to blood flow in an artery, which would explain the reduced overall velocity in recorded traces. Shipley *et al.* used an adjustable type of orifice-meter, in which the orifice size was altered until 'the constriction necessary for desired sensitivity was obtained'. This would seem to be a subjective estimate, and it may be that different settings of the orifice might give different results; but there are no traces or figures of blood velocity in conditions in which only the size of the orifice was altered. As has been seen above (Fig. 8*a*, *b*), the application of a constriction, such as partial ligation, to the vessel can cause a considerable difference in both flow-rate and pattern. It is considered that the use of an orifice-meter may produce effects similar to those caused by partial constriction of the vessel with a ligature.

Mean flow per minute in the femoral artery has been found to be less than that in the carotid artery, although it is usual to find that maximum or peak flow in the femoral artery is higher than that in the carotid, while the minimum flow is less.

Back-flow has not been observed as a feature of the normal flow in either the carotid or femoral artery, but, on the contrary, has been constantly associated with an increase in the peripheral resistance of the vascular bed supplied by these vessels, as in the experiments in which adrenaline was administered. The introduction of an orifice-meter may reproduce this situation in some measure.

SUMMARY

1. The measurement of blood velocity in unopened arteries with an electromagnetic flow-recorder is described.

2. The method has been found to be reliable; the response curve is linear, and the 'total' instrument, i.e. the electrode assembly plus the amplifier, will respond to a frequency of at least 180 c/s.

3. No evidence has been found that the cuff applied to the artery introduces significant artifacts into records of intra-arterial blood velocity changes.

4. Records are presented of normal carotid and femoral artery blood velocity changes. A notable feature of these traces is the absence of back-flow during the cardiac cycle.

5. Evidence is presented to show that moderate increase in peripheral resistance causes the appearance of back-flow in the intra-arterial velocity patterns; the significance of this is discussed.

6. The administration of adrenaline brings about a reduction in minute volume flow in both the carotid and femoral arteries, and the phasic flow records show unequivocal evidence of negative flow.

We wish to thank Mr D. L. Mawson of Messrs Wm. Jessop and Sons, Ltd. of Sheffield, and Mr A. J. Tyrrell, of Messrs Mullard Electronic Products, Ltd., for the magnets used in this work, and also Messrs J. McCarthy and W. E. Blocksidge of this Department for their assistance in the construction of the apparatus.

The work has been aided by a grant to one of us (T. G. R.) from the Joint Committee on Research of the University of Liverpool.

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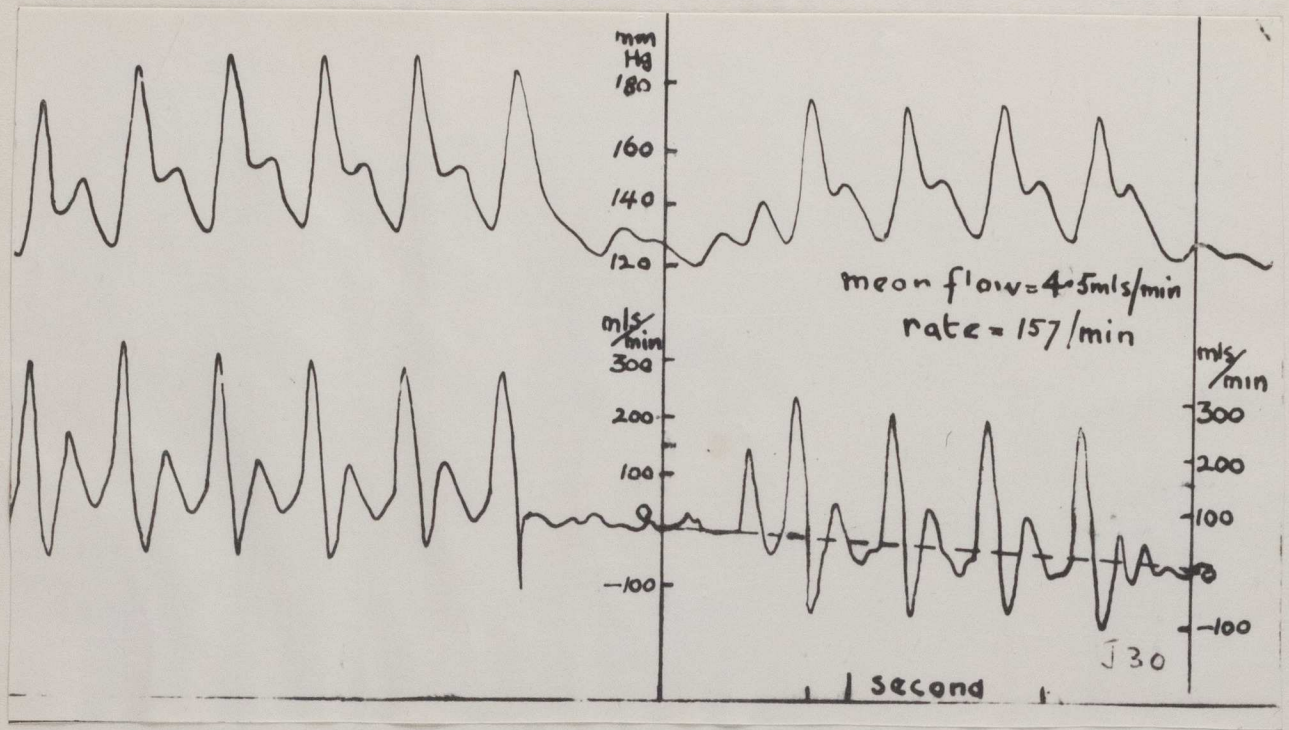


fig 46

These records show the maximal effect of the injection of 2γ of Adrenalin IA

(III) ADRENALINE AND THE COMMON CAROTID

Intra-arterial Adrenaline

Dog	Normal flow ml/min	B.P. mm Hg	Flow after injection ml/min	B.P. mm Hg
J	120.2	170/130	4.5	176/130
J	175.3	176/110	1.57	173/107
G	83.3	141/121	21.8	135/116

Intravenous Adrenaline 50γ

J	155	195/126	37.1	225/199
G	89.3	143/117	19.8	*? /148
G	122.8	141/123	29.9	*? /148
A	174	-	32.9	-

* the systolic pressure was in excess of 250 mm.Hg. for at this pressure the membrane of the manometer touches the insulated electrode.

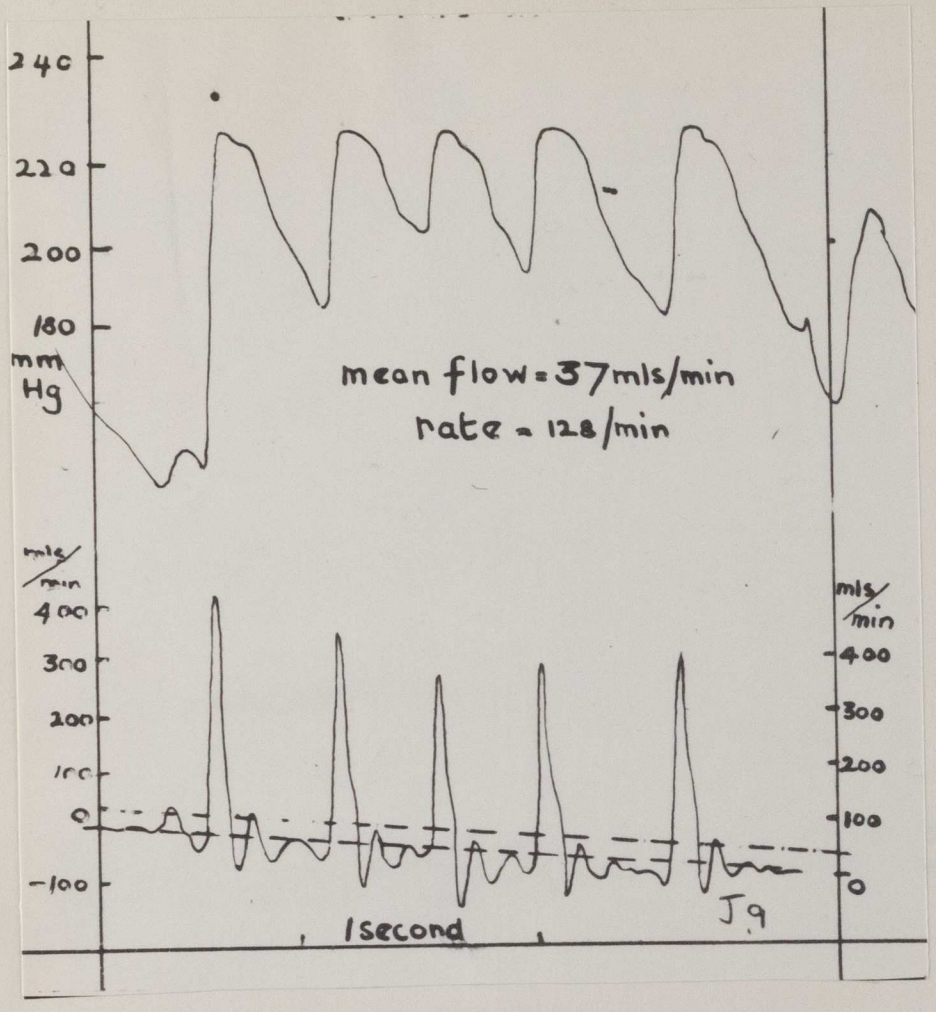


fig 47
Effect of I.V. injection of Adrenaline
Maximal Effect.

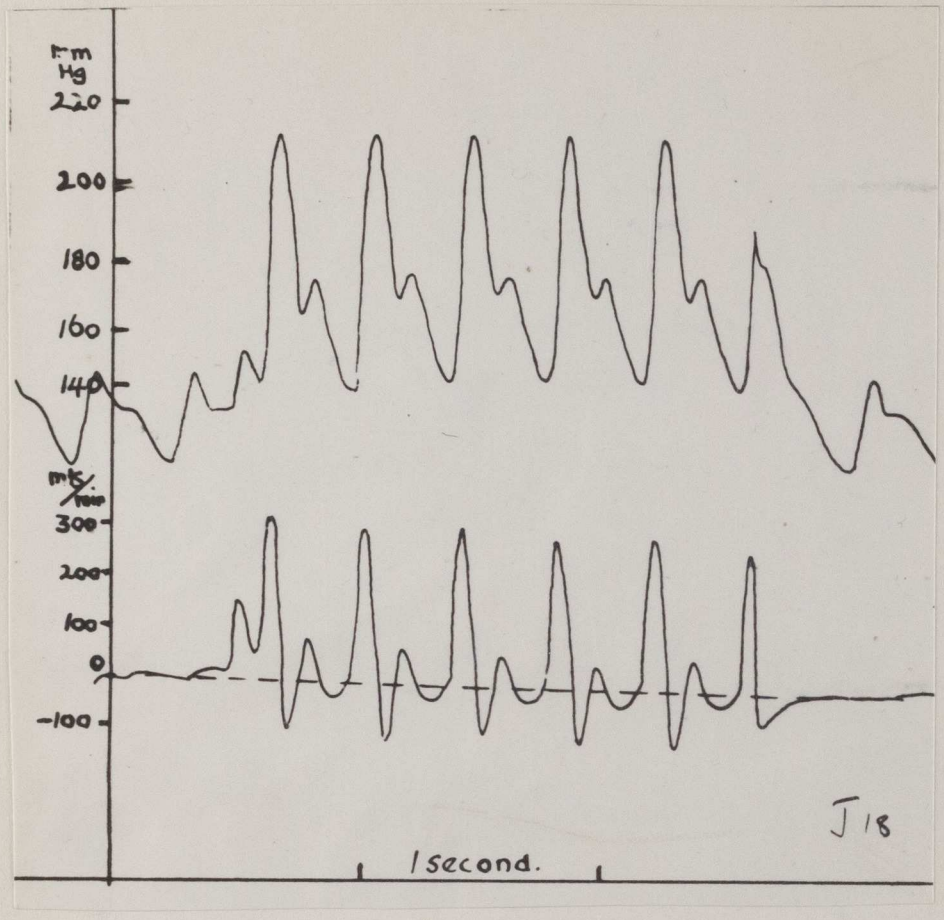


fig 47a.
as fig 47

Adrenaline and Common Carotid blood flow.

Intra-arterial Adrenaline.

Figs.(46) show the effect of an injection into the carotid artery via the recording manometer of 2 γ Adrenalin (Parke-Davis). It will be seen that these curves show no standing flow but that they oscillate about the zero flow line; in fact the mean flow is so small that the mean flow line cannot be drawn in separately from the zero flow line in the figures shown. The systolic velocity peak is large and compares well in amplitude with a normal systolic peak. From the systolic peak the velocity decreases rapidly and becomes negative (backflow). There is then a period of forward flow in excess of the mean and then a further small amount of backflow. The blood pressure and heart rate during these observations were within the normal limits for the animal used, thus showing that the adrenaline had had no effect on the rest of the circulation. Table III gives the results of the flow measurements made. They are all markedly below normal flow levels and it is believed that vaso-constriction took place in the carotid circulation.

Intravenous Adrenaline.

The effect of intravenous adrenaline on blood flow in the common carotid artery is variable. The most usual effect was that shown in Figs.(47 and 47a). This shows a small mean flow with a small degree of backflow. Other records do not exhibit backflow but the mean flow was greatly reduced.

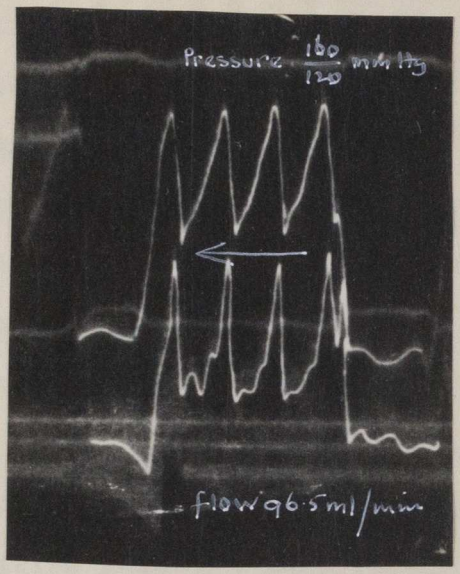


fig 49
Effect of 0.1 γ acetylcholine IA.

IV

EFFECT OF ACETYLCHOLINE ON COMMON CAROTID BLOOD FLOW.

Intravenous Acetylcholine

Dog	Normal		After Ach.	
	flow ml/min	Mean B.P. mm. Hg.	flow ml/min	Mean B.P. mm. Hg.
I(i)	155	145	154	94
I(ii)	102	133	134	110
I(iii)	119	104	85.5	53
G(i)	71.6	130	63.4	120
G(ii)	76.3	131	61.7	112

Intra-arterial Acetylcholine

I(i)	92.5	160	96.5	140
I(ii)	86.5	120	86.3	124
G.	65.7	127	78.3	128

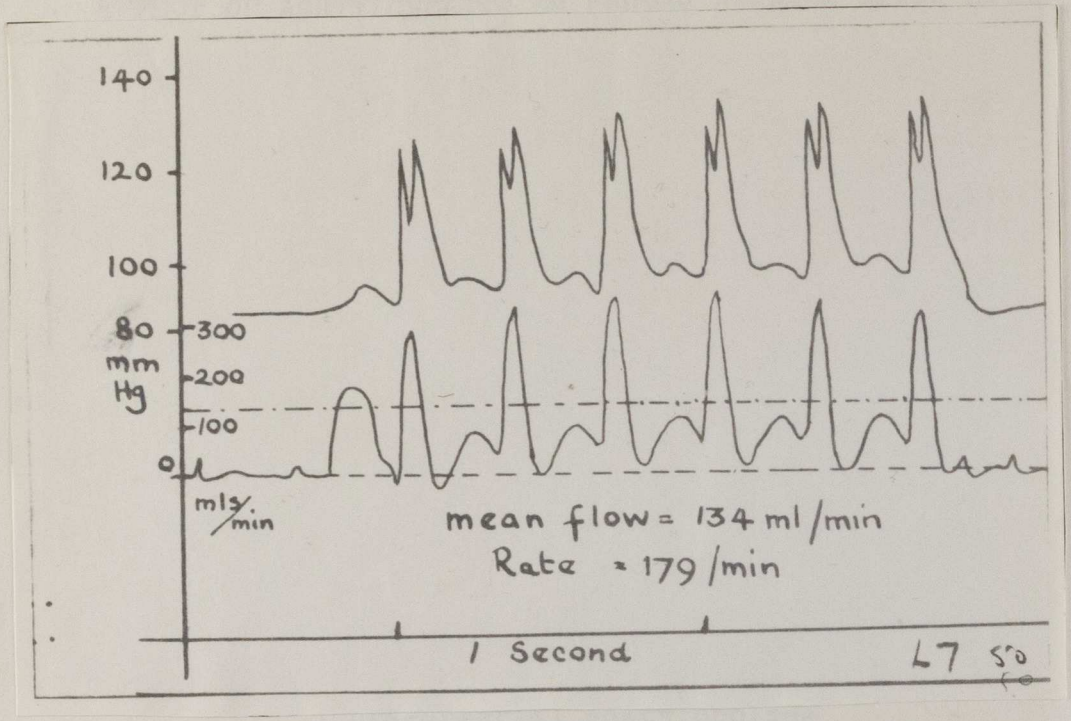


fig 50

Effect of 0.5 mg of acetylcholine I.V.

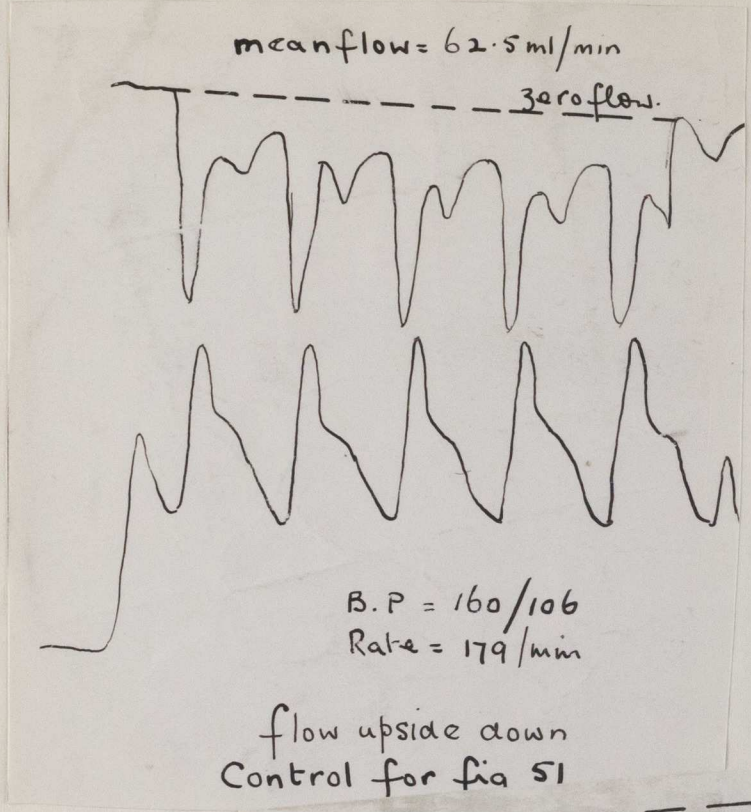
The degree of reduction of mean flow varied from animal to animal but in all cases adrenaline does considerably reduce the blood flow along the carotid artery. The effect is not so great as after intra-arterial adrenaline but it is hardly likely that the local concentration of adrenaline is the same in both cases.

Intra-arterial Acetylcholine and the Carotid Artery.

Typical records obtained after the intra-arterial administration of 0.01 - 0.03γ of Acetylcholine are shown in Fig. (49). The blood pressure values did not fall so that the Acetylcholine did not affect the rest of the circulation but changes were seen in the blood velocity record. The decline in velocity from the systolic peak was continued smoothly into the diastolic part of the velocity wave. The diastolic portion of the wave had a few minor oscillations on it, but if a smooth curve was drawn through these oscillations the velocity curve had the appearance of a logarithmic decline in velocity. Table Iv shows that the blood flow through the artery increased after the intra-arterial injection of Acetylcholine, which caused vasodilation.

Intravenous Acetylcholine and the Carotid Artery.

An anomalous response to intavenous acetylcholine in the case of the carotid artery is shown in Fig. (50) where the velocity curves resemble those obtained with adrenaline. After the systolic peak the velocity fell very rapidly to almost zero, and then it increased to a level above that of the mean flow.



flow upside down
Control for fig 51

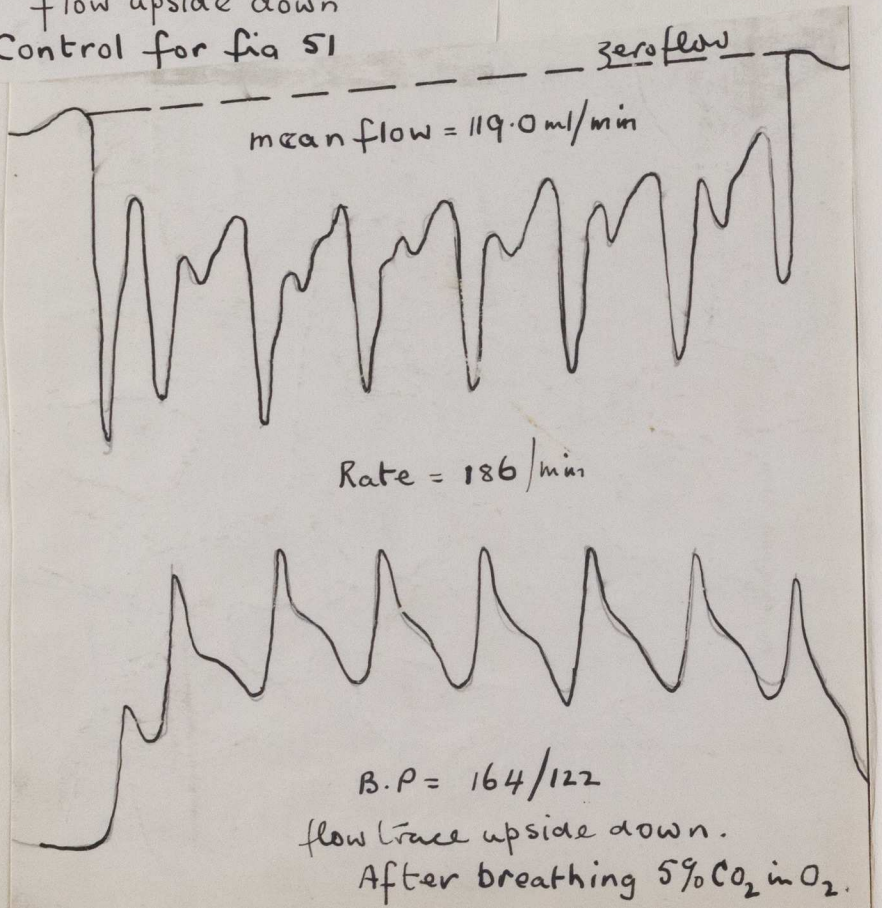


fig 51

V

EFFECT OF CO_2 ON COMMON CAROTID BLOOD FLOW.

Dog	Normal		Breathing 5% CO_2 in O_2	
	flow ml/min.	Mean B.P. mm.Hg.	flow ml/min	Mean B.P. mm.Hg.
H(i)	61.0	132	107.0	143
H(ii)	59.6	130	112.0	147

VI

EFFECT OF STIMULATING THE SUPERIOR CERVICAL GANGLION ON COMMON CAROTID BLOOD FLOW.

Dog	Normal		during stimulation	
	flow ml/min.	Mean B.P. mm.Hg.	flow ml/min	Mean B.P. mm.Hg.
K(i)	94.3	126	42.3	126
K(ii)	118.8	130	70.3	128

The systemic blood pressure fell as would be expected. The total blood flow along the artery also diminished, but this was not unexpected as the cardiac output was more widely distributed through vascular beds dilated by the action of the Acetylcholine. The shape of the velocity record resembled that which is seen after vasoconstriction.

CO_2 and the Carotid Artery blood flow.

Carbon dioxide was administered to the dog by giving it the commercially available mixture of 5% CO_2 in oxygen from a rebreathing bag via a tracheal cannula. The effects of this procedure are seen in Fig. (51). It will be seen there was a well marked increase in flow.

Stimulation of the Superior Cervical Ganglion and the Carotid Artery Blood flow.

The superior cervical ganglion was dissected out on the same side as the blood flow records were made. The ganglion was found by following upwards the combined vagus and cervical sympathetic trunk until the nerve was found to divide and then the sympathetic trunk was followed up until the ganglion was found just beneath the base of the skull. This operation necessitated a large incision and a fair amount of trauma resulted but the condition of the dog remained good. The ganglion was stimulated by a thyratron stimulator giving out a series of oscillations of variable strength and duration, the efficacy of stimulation was judged by seeing whether the

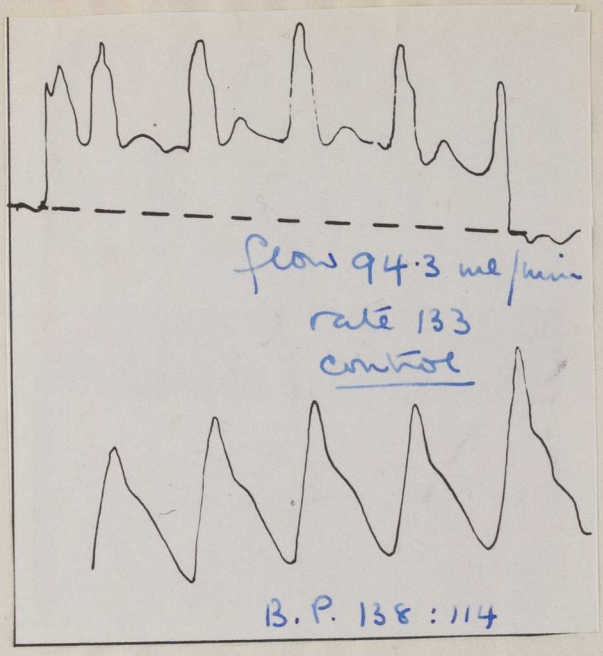
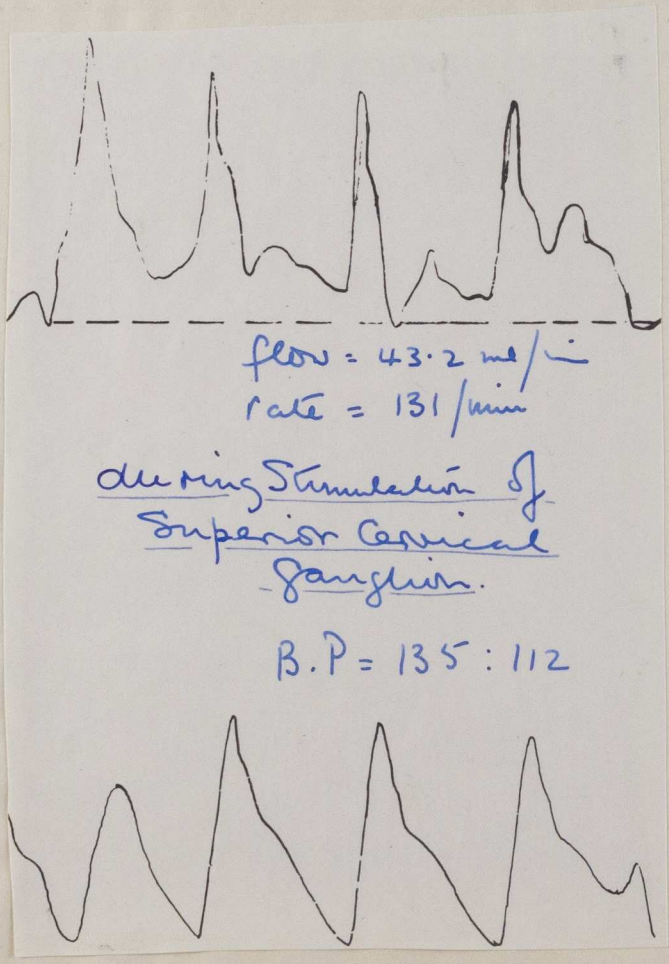

flow 94·3 ml/min
rate 133
control
B.P. 138 : 114

fig 52


flow = 43·2 ml/min
rate = 131/min
during Stimulation of
Superior Cervical
Ganglion.
B.P = 135 : 112

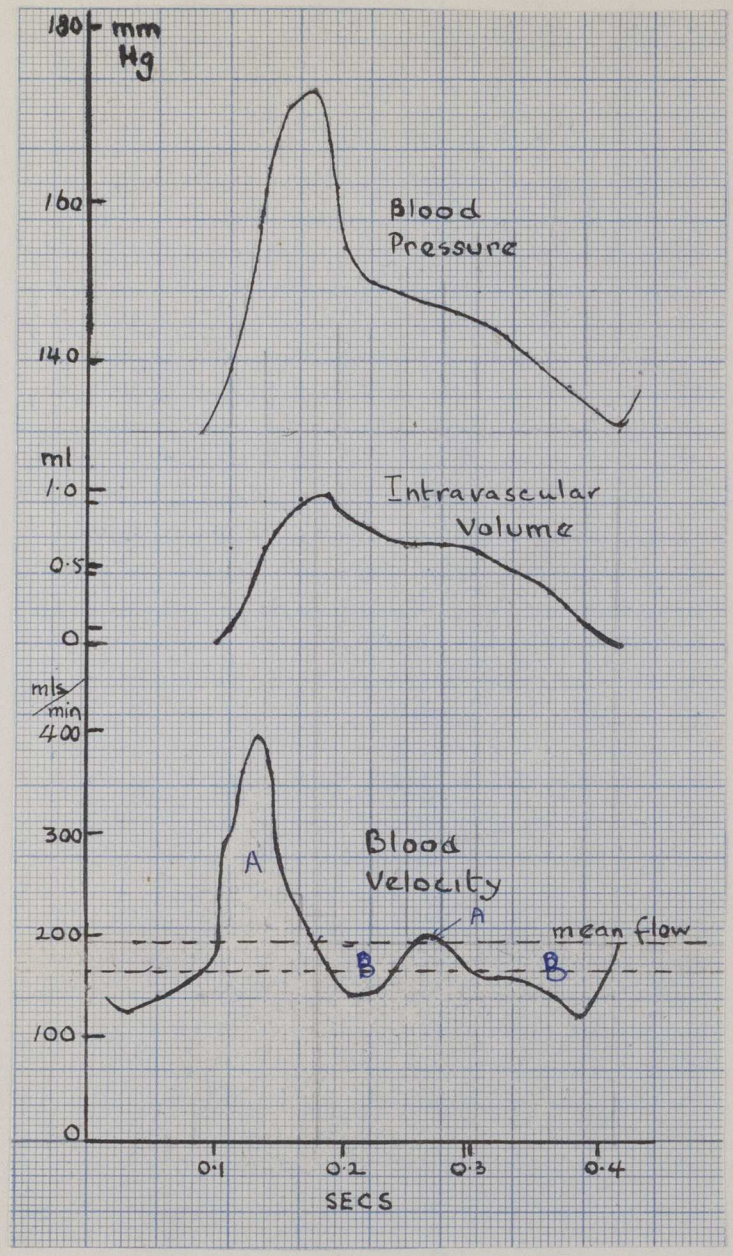

180
mm Hg
160
140
Blood Pressure
ml
1·0
0·5
0
Intravascular Volume
mls/min
400
300
200
100
0
A
Blood Velocity
A
mean flow
B
B
0·1
0·2
0·3
0·4
SECS

fig 53

micitating membrane reacted. Fig (52) is a tracing obtained during stimulation of the superior cervical ganglion and immediately after, and shows the reduction in blood flow. It will be noted that there was little change in the systolic and diastolic blood pressures, as only the peripheral resistance in one part of the animal's circulation was affected, but the form of the wave did alter somewhat. The blood velocity record during stimulation showed a lower mean flow.

When discussing the form of the velocity pulse, Shipley et al, 1943 use an interesting form of analysis. They say that at some point in the vascular bed the flow of blood ceases to be pulsatile and the flow rate is steady because the combined effect of friction and the blood viscosity damp out any variations in flow. It can be assumed therefore, that the out flow from a vascular bed proceeds at a constant rate equal to the mean flow rate along the artery supplying blood to the bed. Fig. 53 shows a blood velocity curve and a line "mean flow" has been drawn. This line is the mean value of velocity above the zero level. The areas A and B are equal. Since A is in excess of the mean flow, the volume represented by the area has been stored in the vascular bed, subsequently to be released as the volume represented by area B. This volume storage effect can be seen more clearly in Fig. (53) where a curve of the volume changes in the vascular bed is constructed by calculating the total inflow into the vascular bed up to the time of the point being determined and subtracting from this

value the amount of blood which will have flowed out of the bed up to this time.

Shipley et al (1943) state that the fluctuations in the velocity pulse are ~~therefore~~ due to the "changes in the rate of flow into the distensible arterial reservoir through which are mediated the corresponding phasic changes in intravascular volume (volume - elastic volume changes within the bed)." They further consider that the areas A & B are a measure of vascular - elastic component of the flow curve, and that since the volume that can be accomodated in the vascular tree during vasoconstriction will be diminished, and that during vasodilation will be increased, therefore the V-E component will decrease in the former case and increase in the latter. To test this hypothesis they studied the flow pattern in peripheral arteries after the injection of vasomotor drugs (Pritchard, et al, 1943), but they obtained some anomalous results. With vasodilator drugs the V-E component in the carotid increased but with adrenaline it also increased even though the mean blood flow fell and the blood pressure remained constant; conditions which are accepted as the conventional signs of vasoconstriction. It would seem therefore on their own results, that the hypothesis they propounded must fall. As the flow velocity curves here produced differ from those of Pritchard et al (1943), the hypothesis was re-tested but the results have no relationship to the vasomotor state of the bed decided by the criteria of change in flow rate with constant blood pressure.

CALCULATION OF PERIPHERAL RESISTANCE

Dog & Expt. No.	Mean flow ml/min.	Mean B.P. mm. Hg.	Peripheral Resistance P.R.U.	
G. 4	65.7	127	1.9	Normal flow
G. 6	83.3	131	1.5	" "
G. 7	71.6	130	1.8	" "
G. 9	76.3	130	1.7	" "
G. 19	11.5	138	12.0	Ext. carotid clipped off
G. 27	8.2	135	16.0	" " "
H. 1	61.0	132	2.2	Normal flow
H. 5	107.0	143	1.3	After breathing 5% CO_2 in O_2
I. 1	92.5	160	1.7	Normal
I. 2	22.8	160	7.0	Ext. carotid clipped off
I. 13a	96.5	140	1.4	1 γ Ach. I.A.
I. 5	86.3	124	1.3	1 γ Ach. I.V.
J. 7	155	160	1.0	Normal
J. 8	25	165	6.6	Ext. carotid clipped off
J. 29	120	140	1.2	Normal
J. 30	5.35	153	28.6	2 γ Adrenaline I.A.
J. 9	37.1	212	5.7	50 γ Adrenaline I.V.
L. 1	154	145	0.9	Normal
L. 2	102	133	1.3	"
L. 7 (i)	154	94	0.7	3 γ Ach. I.V.
L. 7 (ii)	134	110	0.8	3 γ " "
L. 12	85.5	53	0.6	3 γ " "
K. 1	94.3	126	1.3	Normal
K. 8 (i)	42.3	126	3.0	During Stimn. of Sup. Cerv. Gang.
K. 8 (iv)	81.9	123	1.5	5 secs. after stimn.
0. 1	92.1	155	1.7	Common Carotid, Lingual Art. tied
0. 6	22.5	176	7.8	Ditto with ext. carotid clipped
0. 10	35.6	177	4.9	As 01. with 20 γ Adrenaline I.A.

The concept of the Peripheral Resistance Unit.

The vasomotor state of a vascular bed or the peripheral resistance can be expressed in terms analogous to Ohm's Law. The pressure difference across the bed is equivalent to the voltage drop across a resistor (e), the blood flow is equivalent to the current (i), and the resistance offered to the flow of blood is equivalent to the resistance (r). Therefore as in Ohm's Law which is:-

$$i = \frac{e}{r}$$

$$\text{blood flow} = \frac{\text{Pressure drop}}{\text{Peripheral Resistance}}$$

or $$\text{Peripheral resistance} = \frac{\text{Pressure drop}}{\text{blood flow}}$$

The pressure drop is measured in mm. of mercury and the blood flow in ml./min., the peripheral resistance is measured in arbitrary units known as peripheral resistance units or P.R.U. This concept of peripheral resistance measurement is due to Green et al. (1944); they tested it on perfused hind limbs of the dog. It would be of interest to apply this concept to the results described here. Table VII shows the results obtained.

The first point of interest is that the resistance in the normal carotid circulation of different dogs is remarkably constant although the mean flow is very variable. The degree of vasodilation attainable even after large amounts of Acetylcholine intra-arterially, is not nearly as great as the degree of vasoconstriction obtainable after adrenaline. If we accept the fact that large amounts of Acetylcholine in the blood

stream cause a nearly maximal dilation of the peripheral resistance, it would seem that the degree of vascular tone in the bed served by the carotid artery is not very high. But it must be remembered that the flow along an artery is inversely proportional to the fourth power of the radius $\left(\frac{1}{r^4}\right)$, so that an equal decrement in the diameter of a bloodvessel will have a much greater effect than an equal increment. It cannot be expected therefore, that a vasodilator drug will have such an effect on the blood flow through a peripheral resistance as a vasoconstrictor drug. Carbon dioxide reduces the peripheral resistance and stimulation of the cervical sympathetic ganglion increases it. Amongst the results shown are those obtained after clipping off the external carotid artery leaving only the internal carotid artery open. As will be seen this severely cuts down the blood flow and must increase the peripheral resistance as shown in the table.

Green et al (1944) state that the peripheral resistance must be measured at a constant pressure for any changes to be significant. They give a graph showing peripheral resistance plotted against perfusing pressure, and show that the resistance varies with pressure. It is stated that during the experiment the vasomotor tone of the preparation remained constant, but how this was determined is not told. It would seem more likely that the variations in resistance were due to variations in vasomotor tone. For in several experiments it has been found that over very short periods of time, whilst the blood pressure remained constant the blood flow varied and

VIII

P.R.U. FOR SAME MEAN PRESSURE:-

		Mean B.P. (mm. Hg)	Mean Flow mls/min.	P.R.U.
Dog G.4.	A	127	71.5	1.78
	B + 2.5 sec.	127	71.0	1.79
	C + 5.0 sec.	127	68.7	1.85
	D + 9.0 sec.	127	53.5	2.37
	E + 12.0 sec.	127	72.2	1.76

RESULTS OF CLIPPING OFF THE OPPOSITE CAROTID ARTERY.

all results in ml/mm.

Dog	Flow before clipping	Flow after clipping	% change
A	154.3	252	163
B (i)	84	135	161
B (ii)	84	140	166
E (i)	50.5	84.3	167
E (ii)	53.7	79.4	148

hence the peripheral resistance calculated in P.R.U. (Table VIII). Certainly at very low pressures outside the physiological range the smaller blood vessels which constitute the major part of the peripheral resistance are not distended and thereby give a greater resistance to flow. In the normal range of physiological pressures this effect should not be very marked and changes in peripheral resistance can be considered to be due to active vasomotor changes. Even if the peripheral resistance does alter with the pressure, this is still part of the physiological peripheral resistance and cannot be considered as an additive artefact as Green et al (1944) tend to do.

The Effect of Closing off the Opposite Carotid Artery.

It is fair to assume that as the two common carotids in the dog are anatomically symmetrical in their distribution the blood flow up each artery will be about the same. Therefore, if the opposite carotid artery to that from which recordings are being taken is tied off, the head has a blood supply which is deficient by an amount equal to that which is already flowing up the patent artery. The deficit can be made up by the opening up of collateral channels from the other arteries supplying the head of the dog. The results of closing off the opposite carotid artery are shown in Table IX. It will be seen that there is an approximately 60% increase in flow through the open artery. At first it may seem that this result shows that a greater dilation is possible in a carotid bed than is possible after Acetylcholine, but this is not so; the peripheral

resistance has been lowered by the fall in the pressure at the end of the anastomotic channels. This pressure, present in the normal animal, decreases the pressure difference across the anastomotic channels, and hence the flow rate through them. The removal of this source of pressure is clearly equivalent to an increase in mean blood pressure in the side examined.

Distribution of Blood flow between the internal and external carotid arteries.

The blood from the common carotid artery supplies arteries both inside and outside the skull. To physiologists the blood flow in the internal carotid artery is of great interest for it may well give an indication of the state of the cerebral circulation. An attempt was made to put the flow meter on the internal carotid artery in the dog but it is extremely minute and very awkwardly placed at the base of the skull and all attempts failed. It was therefore decided to study the flow of blood along the internal carotid by closing off the external carotid, and measuring the residual flow along the carotid artery. It can be argued that if the external carotid artery is closed off, the main pathway for blood flow along the common carotid is removed, and the conditions therefore at the entrance to the internal carotid will be so changed that the amount of blood flowing along the artery will be different to an important degree from the normal. This point was investigated by first measuring the common carotid blood flow, then the flow after closing the external carotid and then

X

DISTRIBUTION OF BLOOD FLOW BETWEEN INT. & EXT. CAROTIDS.

all results in ml/min

Dog	A. Mean Common Carotid	B. Mean Ext. Carotid	C. Mean Int. Carotid	D. Total of B + C
C	70.0	58	22	80
D	62.3	49	16.3	65.3
O	72.8	53.4	22.3	75.7
M	218.0	203	20.5	221.5

the flow along the external carotid after closing the internal carotid. In theory the two latter measurements should add up to the former. Table X shows the results obtained, and it will be seen that the agreement is satisfactory.

PART III

INTERNAL CAROTID BLOOD FLOW

MEASUREMENT OF THE INTERNAL CAROTID BLOOD FLOW

Introduction

Very few workers have directly measured the internal carotid artery blood flow. Keller (1930), Schneider & Schneider (1934), Gollwitzer-Meier & Eckardt (1935) and Noell & Schneider (1942-4) have used the thermostromuhr to study the internal carotid blood flow in dogs under different physiological conditions. These workers rarely give an absolute value for the blood measurement but express their results in percentage changes from the normal. Winterstein (1935) used the Fleisch stromuhr to measure the internal carotid blood flow in the rabbit; he studied the effects of Adrenaline and Acetylcholine. Dumke & Schmidt (1942) used a bubble flow meter to record internal carotid flow in the Macaque monkey.

The main interest in studying internal carotid blood flow is in its relationship to the cerebral blood flow, Batson (1944) states that the internal carotid artery of the dog is of no value for studying the cerebral blood flow because it plays a minor part in the blood supply to the brain. The vascular anatomy of the brain of the dog is described by Ellenberger & Baum (1891) and Tandler (1898). The brain is supplied by the two vertebral arteries which receive an anastomotic supply from the occipital artery which arises

INTERNAL CAROTID ARTERY FLOW.

Dog		Flow. mls/min.	Mean Flow mls/min.	% of Mean common carotid flow.
Dog B	(i)	9.7		
7.5 Kg.	(ii)	11.0	10.5 mls.	
	(iii)	9.0		
	(iv)	12.3		
Dog D	(i)	15.0		
12.5 Kg.	(ii)	23.0		
	(iii)	23.5		32%
	(iv)	18.0		
	(v)	15.0		
	(vi)	19.0		
	(vii)	21.0		
	(viii)	13.4		
Dog G	(i)	20.9		
12.4 Kg.	(ii)	8.2		
	(iii)	12.0	13.2 mls.	15.5%
	(iv)	11.5		
Dog I	(i)	22.8		
11.5 Kg.	(ii)	9.1	15.9 mls.	16.0%
Dog J	(i)	15.1		
11.2 Kg.	(ii)	34.5		
	(iii)	38.8	25.8 mls.	22%
	(iv)	15.0		
	(v)	24.8		
Dog K	(i)	19.2	14.0 mls.	11.5%
27.0 Kg.	(ii)	8.8		
Dog L	(i)	16.1		
12.5 Kg.	(ii)	32.2	24.1 mls.	19%
	(iii)	24.1		
Dog M	(i)	30.0		
9.0 Kg.	(ii)	30.0	28.2 mls.	15%
	(iii)	22.5		
	(iv)	20.5		
Dog O	(i)	22.5		
9.2 Kg.	(ii)	22.3	22.2 mls.	
		21.8		

from the external carotid, the two internal carotids, and an anastomotic artery called the Internal ophthalmic artery, which arises from the ophthalmic artery which is a branch of the internal maxillary and passes through the orbit to join the internal carotid artery as it joins the circle of Willis. Bouckaert & Heymans (1935) prepared injection specimens of the dog's head and demonstrated the arteries described by the earlier workers. They state that the diameter of the Internal ophthalmic artery is equal to that of the Internal carotid artery.

EXPERIMENTAL RESULTS

The blood flow in the internal carotid artery. Numerous observations were made on the normal resting blood flow along the internal carotid artery by means of the previously described technique of closing off the external carotid artery and tying off the occipital artery. Table XI lists the results. As in the case of the Common Carotid the flow does not bear any relationship to the weight of the dog on which the measurements were made. When the results for the internal carotid flow are expressed as a percentage of the mean external carotid flow no correlation from dog to dog would seem to exist. This is not altogether unexpected for the physical configuration of the heads varied a great deal amongst the dogs used. Possibly if a series of dogs of the same strain or variety were used, better agreement would be obtained.

XII

EFFECT OF STIMULATING THE SUPERIOR CERVICAL GANGLION ON INTERNAL CAROTID BLOOD FLOW.

Dog	Normal		During Stimulation	
	flow ml/min	Mean B.P. (mm Hg)	flow ml/min	Mean B.P. (mm Hg)
K	19.2	135	13.7	133
K	8.8	130	5.3	131
J	15.0	165	10.9	167
J	15.1	160	9.4	159
M	30.0	126	23.4	123

XIII

EFFECT OF BREATHING 5% CO_2 IN O_2 ON INTERNAL CAROTID BLOOD FLOW.

H	20.3	151	26.7	156
H	23.7	154	27.2	157
G	8.2	135	12.5	143
G	12.0	137	14.3	141
O	22.5	170	27.4	183
O	22.3	171	26.9	179

EFFECT OF ACETYLCHOLINE ON INTERNAL CAROTID BLOODFLOW.

Intravenous Acetylcholine

Dog	Normal		After ACH	
	flow ml/min	Mean B.P. (mm Hg)	flow ml/min	Mean B.P. (mm Hg)
L	16.1	150	12.3	123
L	24.1	162	19.7	118
M	30.0	129	19.4	93
D	15.0	-	12.3	-
B	11.0	-	7.6	-

Intra-arterial Acetylcholine

L	32.2	173	36.6	174
M	22.5	127	28.4	125
D	21.0	-	27.3	-
B	9.0	-	13.4	-

Effect of stimulation of the superior cervical ganglion on internal carotid blood flow.

Stimulation of the superior cervical ganglion by the same method as was used when measuring external carotid blood flow caused a decrease in internal carotid blood flow. (Table XII).

Effect of carbon dioxide on the internal carotid flow

A mixture of 5% carbon dioxide in oxygen was given from a rebreathing bag to the dogs through a tracheal cannula. The effect of the carbon dioxide was to raise slightly the blood pressure and to raise the internal carotid blood flow, the percentage rise in blood flow was greater than that of the blood pressure. (Table XIII).

Effect of acetylcholine on the internal carotid flow.

Doses of 0.01 - 0.02µgm of Acetylcholine I.A. had marked effects on the internal carotid blood flow but no effect on the systemic blood pressure. When larger doses of Acetylcholine were given intra-arterially or intravenously the systemic blood pressure fell and with it the internal carotid blood flow. (see Table XIV).

Effect of Adrenaline on the internal carotid flow.

When adrenaline in doses of about 0.5µgm to 1.0µgm were given intra-arterially it had no effect on the systemic blood pressure. Larger doses had an effect on the general blood pressure. Repeated attempts to elicit an effect on the internal carotid flow without causing a rise in systemic pressure

EFFECT OF ADRENALINE ON INTERNAL CAROTID BLOOD FLOW

Dog	flow mls./min.	Mean Press. mm. Hg.	Peripheral Resistance (P.R.U's)	Remarks
D (i)	13.4	-	-	Control for D (ii)
D (ii)	29.3	-	-	5 γ Adrenaline I.V
G (i)	11.5	138	12.0	Control for G (ii)
G (ii)	16.8	250	14.9	5 γ Adrenaline I.V
G (iii)	20.9	115	5.5	Control for G (I.V
G (iv)	21.8	135	6.2	1 γ Adrenaline I.A
I (i)	22.8	117	5.1	Control for I (ii)
I (ii)	25.9	165	6.4	1 γ Adrenaline I.A
J (i)	24.8	165	6.6	Control for J (ii)
J (ii)	24.3	200	8.2	25 γ Adrenaline I.V
J (iii)	38.8	167	4.3	Control for J (iv)
J (iv)	25.9	176	6.8	2 γ Adrenaline I.A

XVI

COLLATERAL CIRCULATION EFFECTS ON INTERNAL CAROTID ARTERY

All results in mls./min.

Dog	Normal	Opposite Ext. Carotid Clipped	Opposite Int. Carotid Clipped	Opposite Common Carotid	Basilar Artery Clipped
B (i)	9.7	-	-	33.5	-
(ii)	12.3	-	-	31.0	-
C (i)	21.0	-	-	37.0	-
D (i)	19.0	-	-	29.4	-
B (i)	9.0	-	15.3	-	-
C (i)	17.4	-	25.3	-	-
(ii)	19.3	-	26.1	-	-
D (i)	18.0	-	24.2	-	-
(ii)	23.5	-	30.7	-	-
C (i)	22.3	30.5	-	-	-
D (i)	23.0	27.8	-	-	-
(ii)	15.0	22.1	-	-	-
Q	21.3	-	-	-	26.5
R	17.8	-	-	-	23.6

failed. Even when the systemic blood pressure was increased the blood flow along the internal carotid artery increased by a very small amount. (Table XV).

Collateral circulation and the internal carotid.

The effect on internal carotid blood flow of clipping off various arteries which supply the head was investigated. The results obtained are given in Table XVI. The basilar artery was exposed as it joined the circle of Willis. The operative technique used was that described by Aschner (1912) & McClean (1928). This method is to approach the base of the brain from the mouth, cutting through the soft palate and drilling the base of the skull. On opening the dura mater the basilar artery is clipped with a silver clip of the type used by neurosurgeons. After practice on several dead dogs the technique was found to be fairly easily performed and relatively bloodless. The description of the technique given by McClean & Aschner is very adequate, but one warning is necessary. After having started to drill there is a tendency to drill downwards into the thick bony ridge of the pterygoid bone behind the pituitary fossa. This leads to a very deep hole which opens on the brain surface too far forwards. The correct direction to drill is downwards and backwards, -for, in a dog lying on its back the surface of the pons is almost vertical.

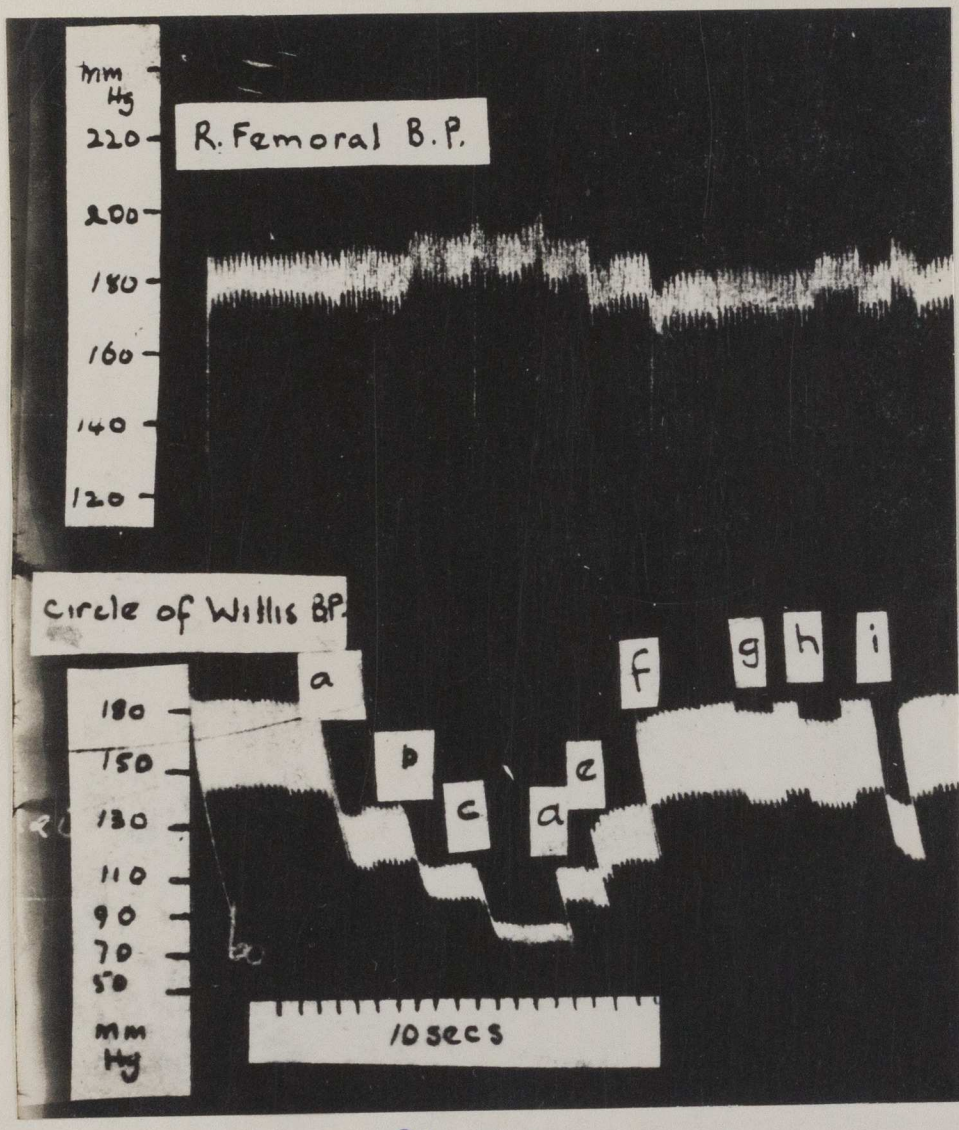


fig 55

a and i = external carotid on recording side off
b and h = " " " opposite " "
c and g = internal " " " " "
d = internal " " " " on
e = external " " " " on
f = external " " recording " "

The blood pressure in the circle of Willis.

In the experiments where blood flow along the internal carotid artery was being measured after clipping the external carotid artery, it was noticed that when the common carotid was clipped between the flow meter and the manometer to obtain zero flow level, the manometer continued to record pressure pulsation. At first it was thought that these pulsations were due to blood leaking past the clip on the common carotid, but on investigation it was found that if the carotid was tied off the pulsations were still recorded. It was then realised that these pulsations were due to the pressure fluctuations in the Circle of Willis being transmitted down the internal carotid, since they ceased on clipping off the internal carotid.

It was decided to take advantage of this observation to investigate pressure changes in the Circle of Willis. To record the pressure in the internal carotid a condenser manometer was tied into the internal carotid, pointing towards the circle of Willis. For experiments of this type a membrane manometer is essential, for a mercury manometer, with its large changes in volume for a given pressure change would seriously affect the dynamics of the cerebral circulation. The most significant results are those where the different arteries supplying the circle of Willis are clipped off (Fig.55). It will be seen that clipping off the external carotid on the opposite side has the same effect on the pressure as clipping off the internal carotid artery on the opposite side.

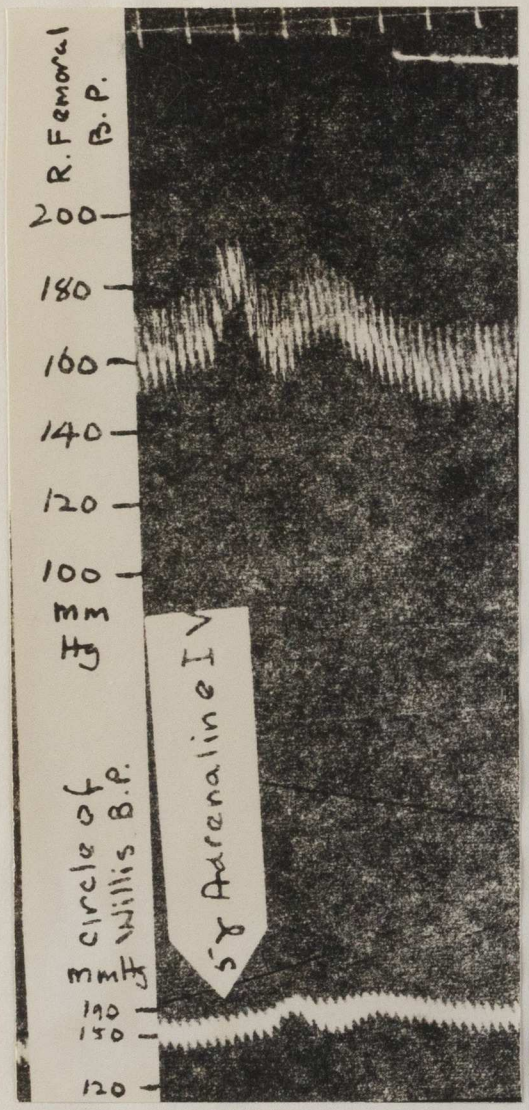

R. Femoral B.P.
200
180
160
140
120
100
mm Hg
3 circle of Willis B.P.
mm Hg
190
150
120
5γ Adrenaline IV

fig 56

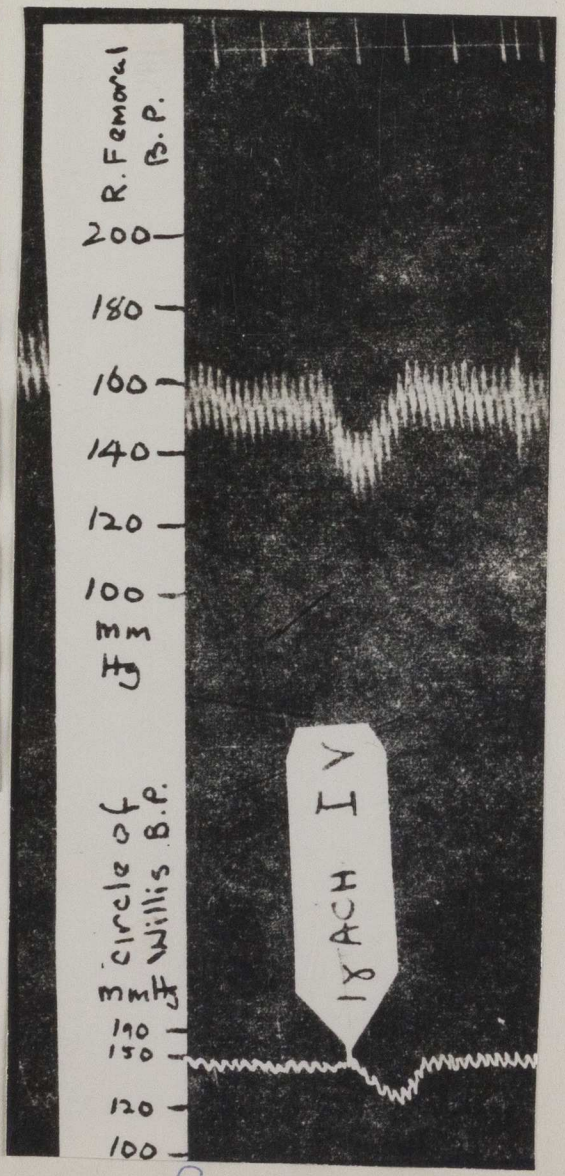

R. Femoral B.P.
200
180
160
140
120
100
mm Hg
3 circle of Willis B.P.
mm Hg
190
150
120
100
1γ ACH IV

fig 58

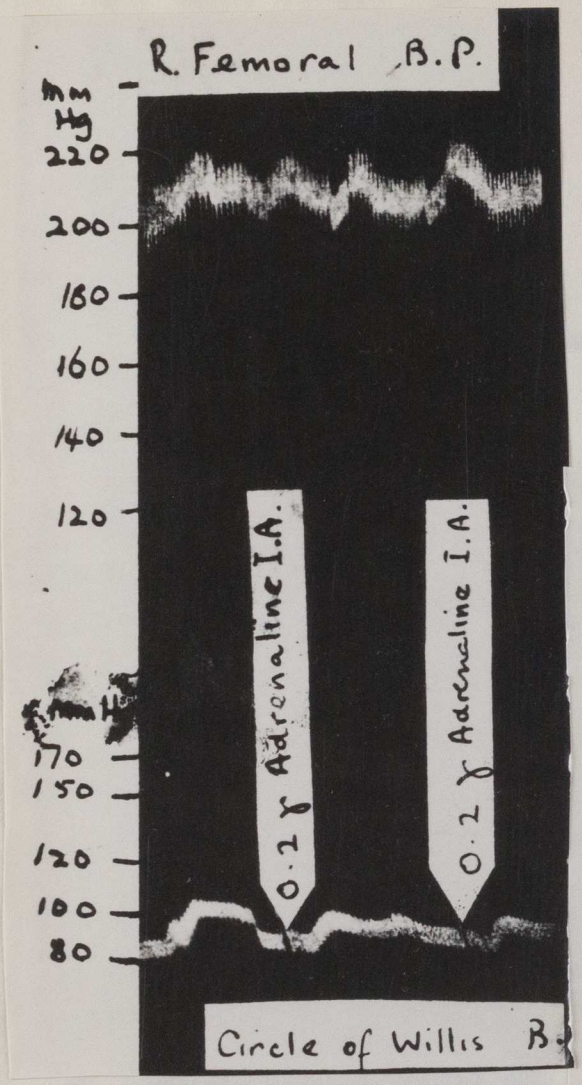

R. Femoral B.P.
mm Hg
220
200
180
160
140
120
mm Hg
170
150
120
100
80
0.2 γ Adrenaline I.A.
0.2 γ Adrenaline I.A.
Circle of Willis B.

fig 59

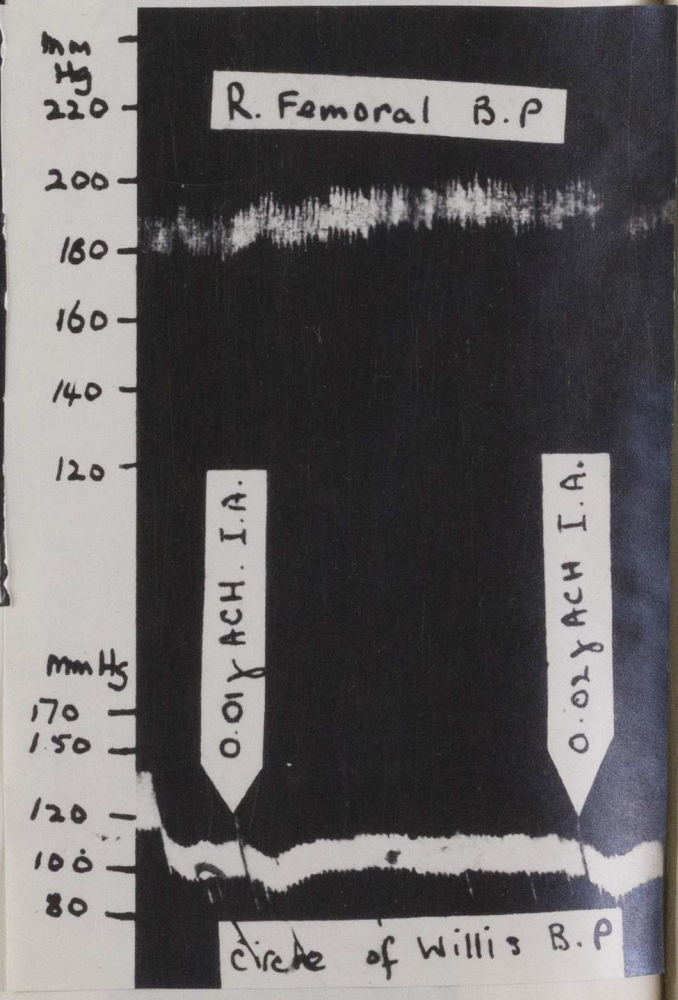

mm Hg
220
200
180
160
140
120
R. Femoral B.P
mm Hg
170
150
120
100
80
0.01 γ ACH. I.A.
0.02 γ ACH I.A.
Circle of Willis B.P

fig 57

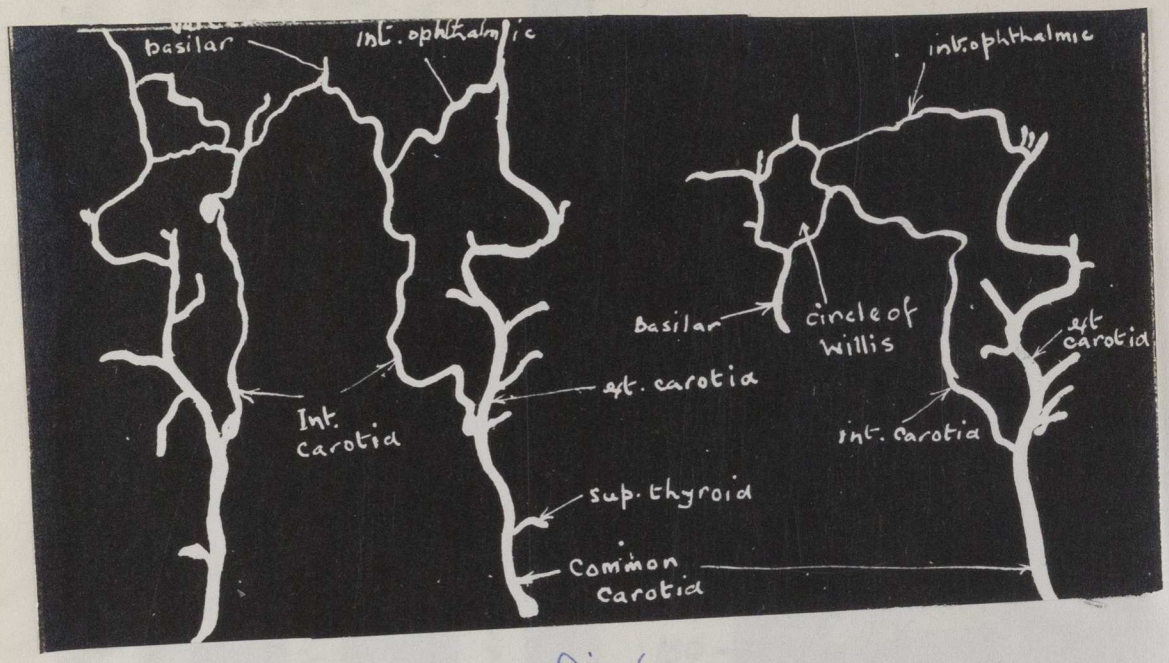


fig 60a

Key to fig 60b.

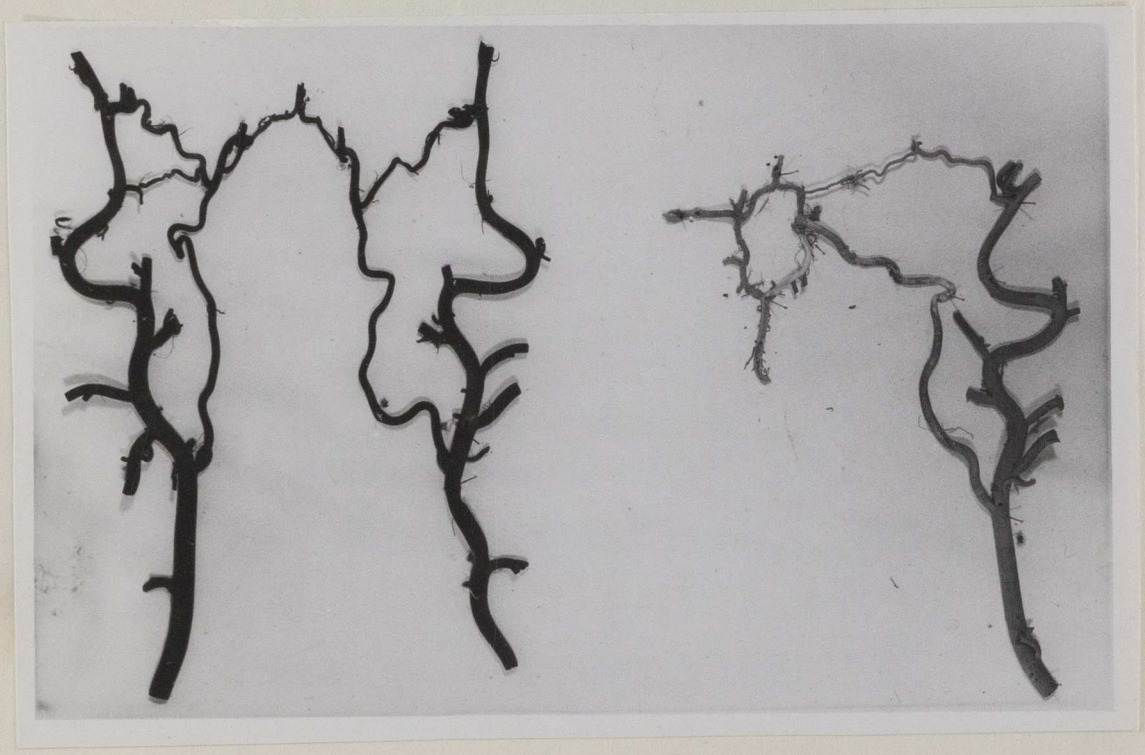


fig 60b
for key see fig 60a

Experiments were carried out to study the effect of drugs on the pressure within the circle of Willis. Acetylcholine given intravenously cause the systemic blood pressure and the circle of Willis pressure to fall together (Fig. 58). When 0.01γ of Acetylcholine was given through the manometer the general blood pressure remained unaltered but the pressure in the circle of Willis fell. (Fig. 57). In the case of Adrenaline when given intravenously the general blood pressure rose and also the pressure in the circle of Willis (Fig. 56). No effect on the circle of Willis without raising the general blood pressure could be elicited when Adrenaline was given in varying doses intra-arterially (Fig. 59).

The Anatomy of Blood Supply to the head.

The vascular anatomy of the head was displayed by gross dissection and by means of neoprene casts of the arteries. The neoprene casts were made by first washing out the blood vessels of the head via the common carotid on one side and the jugular veins on the other side. The washing solution used was 5% gum arabic in saline, normal saline was found to be useless for it made the tissues so oedematous that perfusion became very difficult. The neoprene was perfused under about 250mm.Hg. of pressure and then the head removed and macerated in concentrated hydrochloric acid. Fig. 60a + b are drawings and photographs of the preparations. It will be seen that the internal ophthalmic artery is demonstrated. The two injection preparations illustrated show the two variants observed in the

internal ophthalmic arteries. One shows the internal ophthalmic of about equal size joining with the internal carotid artery, the other a smaller internal ophthalmic carotid artery, joining directly with the circle of Willis.

Effects of Raising the intracranial pressure.

A hole 1/4" diameter was bored into the parietal region of the dog's skull, the dura incised and a cannula screwed into the bone. The cannula was filled with saline and connected through a stopcock to a saline filled pressure bottle. The pressure in the bottle was raised to about 250mm.Hg. and whilst recording blood flow, the pressure bottle was connected to the cannula by opening the stopcock and then released after about 10 secs. The blood flow in the common carotid, the internal carotid and the external carotid arteries was recorded in different experiments during this manoeuvre. These experiments had two aims: namely, to investigate the circulation in the internal carotid and the external carotid arteries via internal ophthalmic artery, during and after a concussive shock. The internal ophthalmic artery joins the internal carotid artery extradurally in the bone of the skull and if the pressure exerted on the arteries of the circle of Willis is greater than the systolic pressure they will close. Hence any blood flowing along the internal carotid artery will not be going to the brain but along the internal ophthalmic artery to the external carotid circulation.

XVII

EFFECT OF RAISING INTRA-CRANIAL PRESSURE

Pressure applied = 250 mm. Hg. in all cases.

Dog	Artery	Before	During	After
K. 14	Common Carotid	188.4 cc/min.	184.2	197
M. 11	Common Carotid	243 cc/min.	214	107
M. 13	Ext. Carotid	125 cc/min.	110	123 → 116 →
M. 14	Common Carotid	121 cc/min.	91	84.5 → 57
M. 15	Int. Carotid	20.5 cc/min.	18	25.5
M. 16	Ext. Carotid	83.0 cc/min.	104	88 → 111
N. 9	Common Carotid	147.0 cc/min.	120	130 → 99.8
N. 11	Int. Carotid	23. 3 cc/min.	19.6	28.7

The results obtained are given in Table XVII. Comparatively few determinations were made as the dogs did not take the procedure very well. The results obtained were unexpected, for very little reduction took place in the blood flow when the intracranial pressure was raised, and if the results could be taken as correct the total blood supply to the circle of Willis from the internal and external carotids would be about 10-20 mls./min. However, it was found that the blood supply to the circle of Willis was not completely cut off by this procedure. When the external carotid was closed off and the common carotid was clipped to obtain zero flow, the condenser manometer showed pressure fluctuations that were coming down the internal carotid. These pulsations must have been of intracranial origin for, in the experiments performed with the manometer in the internal carotid artery, if the common carotids were clipped on both sides during the time the intracranial pressure was raised, pressure fluctuations were still seen which must have had their origin in the basilar artery.

Discussion of Internal carotid flows.

The first problem that has to be discussed is whether the blood flow along the internal carotid artery is a reflection of the vasomotor state in the cerebral circulation. The difficulty is to assess the part played by the internal ophthalmic artery in the cerebral circulation. The opinion expressed by Schmidt (1944) that it is useless to regard the internal carotid flow as a measure of changes in cerebral

blood flow, because of the presence of the internal ophthalmic artery, is thought to be rather severe, for it can be shown that manoeuvres which affect only the circle of Willis, i.e. clipping off the opposite internal carotid artery, have a marked effect on internal carotid flow.

Another noteworthy observation is that, when the recorded blood flows from the external and internal carotid arteries are added together, the common carotid blood flow is only exceeded by a small amount (Table X). If the blood flow along the internal carotid artery was greatly enhanced when the external carotid was clipped, because blood flowed along the anastomosis between the two arteries, the total of internal and external carotid flow would greatly exceed that along the common carotid. In fact it is only exceeded by two or three mls./min.

Admittedly the final proof would be to ligate the internal ophthalmic artery; this has been attempted on many occasions but the great amount of trauma necessitated to expose the artery leaves the animal in such a poor condition that the circulatory reactions of the animal are decidedly unphysiological. Handley et al (1943) state that they were able to approach the internal ophthalmic artery from the mouth, but all attemps to perform this operation led to such profuse haemorrhage from vessels in the bone that the dog's blood pressure fell to extremely low values.

Finally as was shown in the anatomical preparations made

of the internal ophthalmic artery the size of the artery varies a great deal in different dogs. If the amount of blood flowing along the anastomosis was a controlling factor in internal carotid flow, it would be expected that results would vary from dog to dog. This is not the case. It is thought therefore, that a study of the internal carotid blood flow gives a good indication of the changes in the cerebral circulation.

The internal carotid supplies the circle of Willis, and from the circle, vessels supply the brain. The blood from the internal carotid was shown by Kramer (1912) to supply the whole of the ipsilateral cerebral hemisphere and a small part of the frontal region of the other. This work was repeated by injecting 1 ml. of a saturated solution of methylene blue and killing the animal immediately afterwards. The findings agreed with those of Kramer. Shenkin et al (1948) injected Evans blue into the carotid arteries and collected blood from the external and internal jugular veins and they found that the internal carotid blood stays almost wholly on the same side and is drained by the internal jugular vein which does not receive extra cerebral blood. This divided character of the circle of Willis is further illustrated in the experiments which record the circle of Willis pressure when the ipsilateral external carotid was clipped. The resultant fall in pressure was much greater than when the contralateral artery was clipped.

Up to the turn of the century the Munro-Kellie doctrine so dominated the outlook of physiologists that it was thought

that the cerebral circulation was entirely passive. This hypothesis was first postulated by Munro (1783) and developed by Kellie (1824) and stated that, as the brain substance is incompressible and enclosed in a rigid container, the volume of blood contained must remain nearly constant and therefore any increase of flow into the brain must be accompanied by an equal amount flowing out. From this the nineteenth century physiologists presumed that the blood vessels of the brain could exhibit no vasomotor activity and that all changes in cerebral flow were passive. This viewpoint is summarised in Schafer's textbook (1898) & Bayliss & Hill (1895). Gulland in an appendix to the paper of Bayliss & Hill states that using all the neurohistological methods known he failed to demonstrate any nerve supply to the cerebral blood vessels, and it could be presumed that they had none.

The view that the cerebral circulation was wholly passive was soon questioned. Indeed as early as 1858 Claude Bernard showed that when the cervical sympathetic nerve was cut, the temperature of the cortex on the same side was increased. Arloing (1889), using a Chauveau flow meter showed that in the ass the internal carotid blood flow decreased after stimulation of the cervical sympathetic. Gavazzani (1896) tied a manometer into the internal carotid artery of the dog and recorded the circle of Willis blood pressure. He showed that stimulation of the cervical sympathetic raised the pressure. When the experiments on the circle of Willis already described in this

thesis were first performed, it was thought that the idea was original, but when the literature was searched it was found that it was used by many early workers - Hurthle, (1889), Gavazzani, (1896) and Biedl & Reiner (1900). This ignorance can only be extenuated by a remark made to the writer by the late W.H. Newton who said "If we always read all the literature before undertaking a new piece of work, we would never do any". In 1906-7 Wiggers claimed to show that adrenaline diminished the blood flow through the isolated brain. Dixon & Halliburton (1910) stated that the preparation made by Wiggers did not constitute an isolated brain and when the brain was completely isolated adrenaline caused a slight dilation. Wiggers (1914) repeated his work with the Dixon & Halliburton preparation and still found evidence of vasoconstriction.

The results here described are in general in agreement with those obtained by previous workers. The effect of stimulating the cervical sympathetic nerve was to decrease blood flow without any alteration in blood pressure, thus showing the presence of vasoconstriction. Penfield (1932) and Clarke (1934) describe the presence of non-myelinated nerve fibres in the walls of the cerebral blood vessels. Schmidt and his co-workers (Schmidt, 1934, Schmidt & Pierson, 1934, Schmidt, 1935, Schmidt & Hendrix, 1938) measured the rate of heating of a cooled thermocouple placed in different parts of the brain. This they considered was a measure of the blood flow in the region of the thermocouple. They showed that the rate of heating decreased on stimulation of the cervical

sympathetic. The effect of a piece of metal at temperature of about 0°C is not mentioned by Schmidt; it is also interesting to consider that Claude Bernard (1858) was able to make a similar observation by placing his finger on the cortex. Forbes & Wolf (1928) and Bruch (1936) observed that on stimulating the cervical sympathetic nerve trunk the diameter of the pial arteries decreased. The method of viewing the changes in the diameter of the pial arteries has been used extensively by Forbes and his co-workers to study changes in the cerebral circulation and they have published a large number of papers about this topic. The arteries are viewed through a small window screwed into an opening in the skull, thereby maintaining the integrity of the cranium. Forbes observations were confirmed by Thomas (1936) in the unanaesthetized cat. She put indwelling electrodes around the cervical sympathetic and had a permanent cranial window. Using the thermostromuhr on the internal carotid, Schneider & Schneider (1934) and Gollwitzer-Meier & Eckardt (1935) observed that on stimulating the cervical sympathetic, the blood flow decreased. In the isolated perfused head, Pool et al (1934) found vasoconstriction after cervical sympathetic stimulation. Similar results were obtained from the isolated brain of monkey and cats when perfused at constant pressure by Finesinger & Putnam (1933). Talbot, Wolff & Cobb (1929) found that on injecting methylene blue into the circulation, a smaller amount of staining was found on the same side as the cervical sympathetic nerve stimulated. The only result at variance to all these results is that of Dumke & Schmidt

(1942), who measured the cerebral blood flow in the macaque monkey with a bubble flow meter; no change in blood flow was found on stimulation of the cervical sympathetic nerves.

The effect of excess CO_2 in the blood on the cerebral circulation has been widely studied. As in the present work, all previous authors have found that when the CO_2 content of the blood is raised, the cerebral blood flow is increased. This effect of CO_2 has been shown by Bronk & Gesell (1927), and Schneider & Schneider (1934) using a thermostromuhr on the internal carotid and by Gibbs et al (1935) using the same instrument on the jugular vein. Noell & Schneider (1944) repeated the work of Schneider & Schneider (1934) with the internal ophthalmic artery tied, and obtained the same results. Schmidt found that cooled thermocouples in the brain heated more rapidly when the animals breathed excess CO_2 (Schmidt & Hendrix (1938), Schmidt & Pierson, 1934, Schmidt, 1934). In a very skillfully made perfused head preparation in the living cat, Geiger & Magnes (1947) showed that CO_2 increased the cerebral blood flow. The effect of increasing the amount of CO_2 in the blood on pial arteries is to increase their diameter (Wolf & Lennox, 1930). Using the modification of the Fick principle described by Kety & Schmidt (1945) these authors (Kety & Schmidt, 1948), show that the blood flow in the human brain is increased after breathing 5% CO_2 in oxygen.

A great deal of work has been done to ascertain the effect of various drugs on the cerebral circulation, and findings have been presented to show that the blood flow was

altered, or that arteries change in diameter, or the cooling rate of thermocouples have varied. These results have been interpreted as evidence that local vasomotor changes have taken place, although at times no systemic blood pressure record has been presented or if it has been reported, violent changes have occurred in systemic blood pressure. Results of this nature are liable to be very misleading, for, as the earlier physiologists were at great pains to point out, large changes in local vascular conditions can be a passive response to changes elsewhere. The ideal method of investigating vasomotor activity is to attempt to maintain the blood pressure at a constant level and to see if the blood flow alters. If any other variable besides blood flow is measured it must be related to blood pressure.

Descriptions of the effect on the cerebral circulation of Acetylcholine are given by Schmidt & Hendrix (1938), Schneider & Schneider (1934), Wolff (1929) and Winterstein (1935). Schmidt found that a cooled thermocouple in the brain was warmer after the intra-arterial injection of Acetylcholine in small quantities which did not alter the blood pressure. Schneider & Schneider used a thermostromuhr on the internal carotid artery and they found that after the Acetylcholine was given intravenously in large quantities (20γ) and when the blood pressure returned to normal: it was found that the blood flow was increased. Wolff (1928) gave intravenous Acetylcholine and found that the pial arteries increased in diameter. Winterstein (1935) using the Fleisch stromuhr in rabbit internal

carotid arteries recorded an increase in blood flow after acetyl-choline. The results obtained after acetylcholine depend on whether the drug is given in small quantities intra-arterially, thereby not affecting the systemic blood pressure, or whether it is given intravenously and affects the blood pressure. In the former case when the B.P. remains constant the blood flow increases whereas the flow decreases after intravenous injection of acetylcholine, but so also does the B.P. If, however, the peripheral resistance is measured in P.R.U. it will be found in both cases that it has decreased, although at first sight the results after intravenous acetylcholine would appear to indicate an increase. These results are of considerable interest for they show that the blood flow through cerebral circulation can be largely modified by conditions in the rest of the circulation and that changes in the cerebral circulation can have little effect on changing these conditions so as to benefit the cerebral circulation to any great extent. The vasodilator effect of acetylcholine on the cerebral circulation is further confirmed by the fact that after acetylcholine the blood pressure in the circle of Willis falls even though the systemic pressure remains constant.

The effect of adrenaline on the cerebral circulation has been for a long period a source of discussion. Vasoconstriction due to adrenaline has been observed by the following methods:- by perfusing the brain, Wiggers, (1906, 1907, 1914) and Finesinger & Putnam, (1933); by recording internal carotid

blood flow, Keller, (1930), Schneider & Schneider, (1934) & Winterstein, (1935); by measuring the internal carotid blood flow with the carotid blood pressure maintained at a constant level, Miwa, Ozaki & Shiroshita, (1927); by changes in the diameter of the pial arteries, Forbes & Wolff (1928), Forbes et al. (1933) and Florey (1925); by temperature changes in a cooled thermocouple, Schmidt & Hendrix (1938); by a rise in the blood pressure of the circle of Willis, Biedl & Reiner (1900). In the present experiments it was not found possible to give intra-arterial adrenaline in amounts which did not affect the blood pressure whilst at the same time altering the blood flow along the internal carotid artery. Similarly when the pressure in the circle of Willis was measured, any dose of adrenaline which affected the circle of Willis pressure affected the systemic blood pressure. The results obtained after intravenous and intra-arterial injections were similar, the blood flow along the internal carotid artery remained almost constant, whilst the blood pressure increased. If the response of the cerebral circulation was passive it would be expected that the blood flow would increase with such an increase in blood pressure. As the flow does not increase it must be that it is prevented by some active mechanism. If the peripheral resistance is calculated it will be seen that it increases. Thus it can be concluded that adrenaline causes vasoconstriction. One reservation must be made; it is possible that the active vasoconstriction is due not to the adrenaline directly, but to some reflex vasoconstriction caused by the raised blood pressure.

Experiments were not carried out to test this hypothesis, but before any definite conclusion can be arrived at they must be performed, or some method can be devised to prevent the rise in systemic blood pressure caused by the adrenaline.

The effect of clipping the contralateral internal carotid artery on the blood flow along the ipsilateral internal carotid artery has been described by Schneider & Schneider (1934). They demonstrated that the blood flow along the internal carotid artery was increased if the external carotid was clipped; this was interpreted as a reflex originating in the internal maxillary artery. These workers did not realise that the internal ophthalmic artery existed and was a branch of the maxillary artery. This error was pointed out by Bouckaert & Heymans (1935). The present results show that the external carotid artery has a functional communication with the cerebral circulation and that clipping it has an effect on the contralateral internal carotid blood flow and the circle of Willis pressure equal to clipping off the internal carotid artery. Schneider & Schneider (1934) also clipped off the vertebral arteries and stated that this manoeuvre had only a very slight effect on internal carotid blood flow. Batson (1944) states that large anastomoses exist between the vertebral arteries and the arteries of the neck and the occipital artery. If the basilar artery is clipped off just before it enters the circle of Willis, the results obtained disagree with those of Schneider & Schneider and show that an effect equal to about 75% of the effect of clipping of an internal carotid artery is elicited. From this

experiment it is concluded that the circle of Willis derives part of its blood supply from the vertebral-basilar artery circulation.

The experiments carried out (Tables XVII) on the effects of raising the intra-cranial pressure, were a disappointment. It had been hoped that by means of this manoeuvre all the blood supply to the brain could be cut off, but the circle of Willis was not completely collapsed. Eyster et al (1909) performed a similar experiment and obtained similar results. They recorded the outflow from the isolated brain circulation in the dog with the intra-cranial pressure raised above the systolic pressure and found that the outflow was reduced by only 50%. It would seem therefore that some blood is able to reach the circle of Willis despite the raised intra-cranial pressure. A possible cause is that when a cannula is put into the parietal region of the skull, the brain is pushed downwards by the increased pressure, and a region of reduced pressure exists beneath the curved lower surface of the brain.

Suddenly raising the intracranial pressure is similar to the effect of a penetrating injury to the skull and possibly similar to a concussive blow. Scott (1940) shows that when a dog's skull is given a concussive blow, the intra cranial pressure momentarily reaches 300 mm.Hg. Scott suggests this is the cause of the concussive reaction of the brain. Denny Brown & Russell (1941) using monkeys and cats, consider that the reaction is due to the sudden violent movement of the skull

in relation to the brain but that in a penetrating wound the raised pressure causes the concussion. Denny Brown & Russell (1941) show that the effect of suddenly raising the intra-cranial pressure in the cat is a decrease in systemic blood pressure and a condition similar to that obtained after a blow on the head. These authors also show that after a concussive blow on the head in a monkey, the outflow from the internal jugular vein is increased. The results in the present work are in agreement with those of Denny Brown & Russell in that after the intra-cranial pressure has been suddenly raised and then released, the blood flow along the internal carotid artery is increased, but later the flow is decreased.

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SUMMARY

1. Methods of measuring intrarterial blood flow are discussed.

2. An electromagnetic flow meter is described.

3. Methods of measuring blood pressure are discussed.

4. A condenser manometer is described.

5. A multichannel recording galvanometer is described.

6. The velocity pulse wave in the common carotid of the dog is described and it is shown that under normal circumstances back flow does not occur.

7. It is shown that adrenaline decreases the blood flow along the carotid artery and causes backflow to occur.

8. Intrarterial Acetylcholine causes an increase in carotid blood flow. Intravenous Acetylcholine causes a decrease in carotid blood flow.

9. Giving the animal 5% CO_2 in O_2 to breathe causes an increase in carotid blood flow.

10. Stimulation of the Superior cervical ganglion causes a decrease in carotid blood flow.

11. The results are discussed in the light of previous work.

12. It is shown that when the blood flow along the carotid is stopped the flow along the other nearly doubles.

13. The rate of blood flow along the internal and external carotid arteries was measured and was found to total that along the common carotid artery.

14. Stimulation of the Cervical Sympathetic ganglion caused decreased blood flow along the internal carotid artery.

15. CO_2 caused an increased internal carotid blood flow.

16. Arterial Acetylcholine increased and Intravenous acetylcholine decreased the internal carotid blood flow.

17. Adrenaline decreased the internal carotid blood flow.

18. The collateral circulation in the circle of Willis was investigated.

19. The blood pressure in the circle of Willis was measured and the effects of drugs on the pressure are described.

20. The Vascular anatomy of the dog's head was studies by means of neoprene casts.

21. The effects of raised intracranial pressure on internal and external carotid blood flow are described.

22. These results are discussed in relation to the previous literature on cerebral blood flow.

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